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CHEMICAL INDUSTRY AND SCIENCE IN THE SIXTH FIVE-YEAR PLAN

The recently terminated Twentieth Congress of the C.P.S.U. will be remembered in history as a congress of triumphant builders of communism, as a congress signaling the newest and highest stage of the battle of the party and the Soviet people to realize the great plan of Lenin for building a communist society.

The report of the Central Committee and the Directives of the Twentieth Congress with respect to the Sixth Five-Year Plan reveal grandiose perspectives for further accelerated progress for our nation in the fields of technology, economy, social, cultural and scientific life, for increasing the well-being of the Soviet people and the might of the socialist state. These perspectives heighten the importance of our party and our Motherland still more in the eyes of the nations of the world and instil in the heart of each Soviet citizen a spirit of legitimate patriotic pride.

Having fulfilled the Fifth Five-Year Plan, the Soviet nation has achieved a powerful new rise in the national economy and further development of heavy industry; on this basis it has achieved a steady growth in agriculture and in light industry and food production. Having maintained outstanding successes in economic and cultural building, the Soviet Union has taken a new formidable step forward along the path of gradual transition from socialism to communism.

The main task of the Sixth Five-Year Plan for development of the national economy of the USSR is, on the basis of preferential development of heavy industry, a continuous technical progress and increase of the productivity of labor to secure the further mighty growth of all branches of the national economy and a sharp increase in agricultural production, and thus achieve a significant increase of the material well-being and cultural level of the Soviet nation.

The Directives on the Sixth Five-Year Plan envision an overall increase of the volume of industrial production of 65%; the manufacture of the means of production should increase approximately 70% and the production of consumer goods, approximately 60%. This means that in 1960, the last year of the Sixth Five-Year Plan, the volume of industrial production will have increased to three times that of 1950.

The most important tasks of the Five-Year Plan in the field of industry require, firstly, advancing the development of ferrous and non-ferrous metallurgy and the petroleum, coal and chemical industries. Up to the Great October Socialist Revolution, the chemical industry of Russia was poorly developed. Although great riches lay hidden deep in the Russian soil, many chemical products were imported to us from abroad. The remarkable discoveries and investigations of Russian chemists found no practical application in the Motherland. Only under the Soviet power did the chemical industry find its place among the leading branches of the national economy. The Party and the State have always given great care to the development of native chemical industry and science. In 1934 the Seventeenth Party Congress set the goal for attaining significant progress in developing the chemical industry and in securing broad application of chemistry in all branches of the national economy. Starting with the Second Five-Year Plan and in subsequent plans, our native chemistry has attained considerable success, especially in the petroleum, coal and shale industries, in non-ferrous and ferrous metallurgy, fertilizers, nitrate industry, synthetic rubber, plastics and synthetic fiber.

Soviet chemists, in collaboration with geologists, have discovered new petroleum deposits. Very valuable investigations were carried out by S. V. Lebedev in the field of synthetic rubber. Due to his investigations, in progress at the start of the thirties, this industry has developed vigorously and has played an important role in the national economy of the USSR. In recent years Soviet chemists have had striking successes. We must first of all note the achievements of Soviet physicists and chemists in the technology of nuclear-fuel preparation and in the chemistry of artifical transuranium elements. Our scientists have recently performed outstanding work in

the field of chemistry and chemical technology.

However, at present, the state of our chemical industry and science cannot satisfy the rapidly growing needs of the national economy. Further development of the chemical industry has now become a very important prerequisite for the technical progress of the USSR. Directives of the Sixth Five-Year Plan for the development of the national economy of the USSR for 1956-1960 envision accelerated tempos of development for the chemical industry and, in particular, for the production of chemical products necessary for ensuring technical progress in various branches of the national economy. The Directives demand: an approximate 70% increase during the Five-Year Plan in the output of factories under the Chemical Industry Ministry that produce ammonia and caustic soda; increase in the production of chemical products that will mean an increase in the harvest of agricultural crops; organization of the production of new types of concentrated mineral fertilizers and new, more effective, chemical poisons against pests and diseases of agricultural plants; and raising the production of concentrated phosphate fertilizers to approximately one million tons a year. Provision has been made for the large-scale production of chemical agents to be used against weeds in order to secure an appreciable decrease in labor costs on agricultural crops and also in order to sharply increase the production of raw materials for mineral fertilizers — apatite concentrate, phosphorites, sulfuric acid and sulfur based on the utilization of natural sulfur deposits, processing of copper-sulfate ores and sulfur-containing gases.

It is necessary to secure rapid rates of development in the production and processing of petroleum, to increase the production of light-petroleum products approximately 100% and the production of lubricating oils 80%. Provision has been made for more intensive processing of petroleum. The quality of motor and tractor fuels and oils must be improved; the anti-knock properties of gasolines must be improved; the sulfur and paraffin content of diesel fuel must be decreased; the body and efficiency of motor and diesel fuels must be improved; new improved technological processes and methods of producing petroleum products must be incorporated in those petroleum-processing factories that are being built and are undergoing reconstruction. It is necessary to develop the gas industry as rapidly as possible, to increase the utilization of gas in the national economy as chemical raw material and fuel and also for daily needs, and to increase production of gas approximately 290% during the five-year period.

One of the most important tasks of the chemical and petroleum industry was considered by the Twentieth Congress to be the necessity for a sharp increase in the utilization of petroleum (natural) gases and petroleum products for the production of synthetic rubber, alcohol, detergents and other chemical products in order to completely replace food products that are used for industrial purposes by synthetic raw materials in the course of the Sixth Five-Year Plan. It is necessary to increase the production of synthetic rubber 120%, and to increase the output of chemicals, due to better utilization of coke oven gas and coal-coking products.

The Directives provide for the expansion of the variety and output of synthetic resins, high-quality lacs and dyes, plastics, electric-insulator materials, synthetic materials for machine-building, electronic and other materials of the national economy, and for an approximately 100% increase in auto-tire production. Provision has also been made for appreciable development of the paper industry; for increase in the production of various types of paper and cardboard, application of progressive methods of digesting cellulose and hemicellulose, hydrolyzing wood, and for increasing the production of hydrolysis and sulfite alcohol by 130%.

In the field of light industry, provision has been made for further expansion of production, improvement in quality and variety of consumer goods, and especially for a broad increase in the output of textile material.

The output of artificial fiber will reach 330 thousand tons in 1960 (of which 44 thousand tons will be synthetic fiber), or five times as much as in 1950. Provision has been made for expansion of scientific research work in the field of production and processing of artificial fiber, synthetic fiber in particular, and a search for methods of decreasing the losses of raw material in the textile and light industries. To attain additional reserves of sugar and vegetable oil, provision has been made for wide application of separation methods for sugar extraction of sugar-beet syrup, and an extraction method for extracting oil from olive seeds.

Provision has been made for further application in chemical industry of new effective technological processes and high-production equipment; for intensive development in the manufacture of instruments for controlling and regulating technological processes, and for the output of high-production equipment for the chemical industry. This is indeed an immense, labor-consuming, but praiseworthy, program of work during the five-year period for chemists, workers and scientists!

The reports of Comrades N. S. Khrushchev and N. A. Bulganin cited the special importance of increasing in every way the production of synthetic chemicals from petroleum products and natural gases to increase the output of artificial fabrics and also food substitutes. This area certainly presents a great task for our scientific research institutes as well as for the factories of the chemical industry, which have given insufficient attention to the development of this important branch of the industrial economy. Natural gases and petroleum products, as chemical raw materials, are still used insufficiently and the task of our scientists is to assist industry in utilizing these valuable resources in the service of the national economy.

The speech of M. G. Pervukhin at the Twentieth Congress of the C.P.S.U. contained justifiable reproaches to chemists, workers and scientists. He directed attention, for example, to the fact that in the past year, of 15 billion cubic meters of coke-oven gas, only 5.3% was used for chemical processing in the preparation of ammonia and organic chemicals. The remainder of this gas was used by metallurgical factories simply as fuel. Meanwhile, it is fully possible from a technical point of view to use a considerable portion of the coke-oven gas as raw material for chemical production. It is very important to more fully utilize ethylene, contained in coke-oven gas, for the production of polyethylene and synthetic alcohol. Thus, the country may obtain a considerably larger quantity of diverse organic chemicals and mineral fertilizers.

Many criticisms were heard from the rostrum of the Twentieth Congress of the C.P.S.U. in the statements of our scientists with respect to many defects in scientific work and in the field of chemistry. Indeed, our country has an immense material scientific base and a multitudinous army of scientists. While in Czarist Russia, where, aside from the Academy of Sciences, only the laboratories of nine universities and several other institutions of higher learning concerned themselves with science, there are now in the USSR almost 800 institutions of higher education, among which stand such giants as the Moscow State University, several thousands of scientific departmental branch institutes of industry and agriculture, a system of public health care, and a science center – the Academy of Sciences of the USSR with its 120 scientific institutes and laboratories and, moreover, thirteen academies of science of the Union Republics. All this offers great possibilities for solution of the principal and most important scientific problems.

Concentrating their efforts, first of all, on the treatment of current scientific problems that are of prime national economic importance, the scientific research institutes and institutions of higher education should reach that level on which scientific problems are treated profoundly and from many sides, in order that these investigations may more rapidly reach completion and the results applied to production. There must be an end to the situation in which the associates and laboratories of various scientific institutions are unproductive for long periods of time with respect to serious scientific production.

The First Secretary of the Central Committee of the C.P.S.U., Comrade N. S. Khrushchev, in his clear report to the Party Congress, expressed the deep gratitude of the people to our scientists for their fruitful work. Gratitude to our native Communist Party and the Soviet people obliges chemists to selflessly work for the benefit of the Motherland and to devote all their efforts and knowledge to the great cause of building Communism.

G. V. Zavarukhin

THERMOGRAPHIC INVESTIGATION OF THE MOST IMPORTANT SATURATED HETEROPOLY ACIDS

E.A. Nikitina and E.V. Buris

Heteropoly compounds are characterized by their considerable water content (up to 30 or more water-of-crystallization molecules in the coordination formula); the works of A.V. Rakovsky and co-workers [1], in which Van Bemmelen's method was used, established that: 1) the water of crystallization forms solid solutions as well as typical hydrates, both of which types are metastable, and 2) a small portion of the water of crystallization and all water of constitution of heteropoly compounds is more firmly bound; thus, over concentrated sulfuric acid phosphotungstic acid retains 6 molecules water of crystallization and all water of constitution; phosphomolybdic acid loses all of its water of crystallization and most of its water of constitution, retaining only 1 molecule of the latter. Over H_2SO_4 silicomolybdic acid retains about 4 molecules of water of crystallization and all of the water of constitution.

Our problem was to determine the stability of the water-molecule bonds in practically important heteropoly acids; phosphomolybdic, phosphotungstic, silicotungstic and silicomolybdic. We thought an investigation of this type might offer new corroboration of the coordination theory of the structure of heteropoly compounds and would establish the thermal stability of the most important heteropoly acids; up to the present this property of the investigated compounds has not been fully ascertained.

EXPERIMENTAL

The heating curves were recorded [2] on a N.S. Kumakov recording pyrometer with a simple and differential recorder. Heating of the investigated samples was carried out in a crucible furnace in which was placed a large crucible filled with powdered Al_2O_3; two small Stepanov vessels which contained the investigated sample and a standard for the differential recorder were placed in the crucible. Al_2O_3, calcined and ground in a mortar, served as the standard. The hot junctions of the thermocouples were placed in the Stepanov vessel; the furnace was insulated on top by asbestos. A chromel-alumel thermocouple was used for the work. The instrument was graduated up to 550°. The recording was continued for 1-1.5 hours; the furnace was heated up at the rate of 2-5° per minute. To determine the nature of the dehydration processes that were taking place, the samples were weighed before and after transformation.

The starting substances were prepared by previously devised methods [3] and were dried in desiccators over H_2SO_4. The first record was of the heating curve of phosphomolybdic acid; the initial preparation contained 13.5 molecules of H_2O. The heating curve of phosphomolybdic acid showed two endothermal effects at 114 and 164° (Fig. 1); as the temperature rose further, the form of the heating curve indicated the presence of the transformation process which proceeded slowly over an extended temperature interval. The meaning of the first endothermal effect at 114° lay in the loss of 7.5 molecules of H_2O by the heteropoly acid; at 114° the acid had the composition $H_7[P(Mo_2O_7)_6] \cdot 6H_2O$. After the second effect at 164°, the acid lost all its water of crystallization and had the composition $H_7[P(Mo_2O_7)_6]$. It is very interesting to note that at the above temperature the complex anion remained intact and the dehydrated acid dissolved completely in water without turbidity.

Further heating brought about the gradual decomposition of the acid. At 270° the acid lost part of water of constitution and had the composition $P_2O_5 \cdot 24MoO_3 \cdot 2H_2O$; at 350° further dehydration took place and more water of constitution was lost; at this temperature the composition of the acid was $P_2O_5 \cdot 24MoO_3 \cdot 1.6H_2O$.

At 450° the acid was completely dehydrated to a sum of oxides $P_2O_5 \cdot 24MoO_3$.

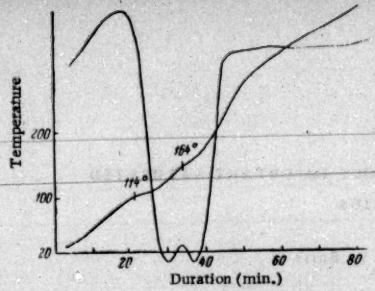

Fig. 1. Heating curve of phosphomolybdic acid.

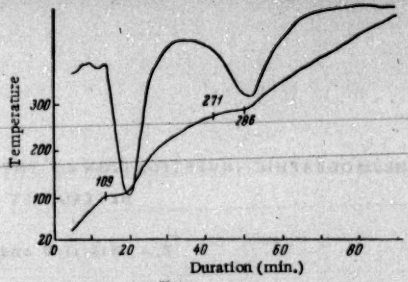

Fig. 2. Heating curve of phosphotungstic acid.

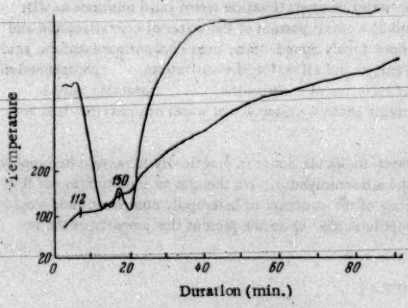

Fig. 3. Heating curve of silicomolybdic acid.

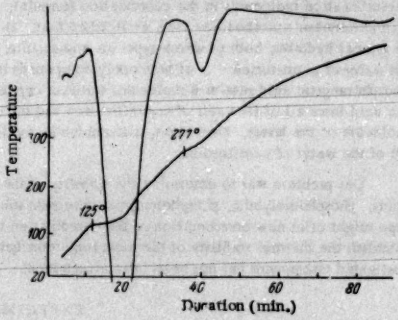

Fig. 4. Heating curve of silicotungstic acid.

Phosphotungstic acid, the thermogram of which we recorded, had the composition $H_7[P(W_2O_7)_6] \cdot 13H_2O$. The heating curve of the heteropoly acid shows two endothermal effects at 109 and 271-286° (Fig. 2). The loss of 9 molecules of water of crystallization took place at 109°; at this temperature the acid existed in the form of the hydrate $H_7[P(W_2O_7)_6] \cdot H_2O$. In the temperature region 271-286° the anhydrous acid formed, which had composition $H_7[P(W_2O_7)_6]$, and gradually decomposed on further heating. On being heated to 380°, phosphotungstic acid lost a large part of its water of constitution and formed a product with the composition $P_2O_5 \cdot 24WO_3 \cdot 1{,}7H_2O$, which upon losing water at 550°, converted to the sum of oxides $P_2O_5 \cdot 24WO_3$.

The silicomolybdic acid which we took for thermographic investigation had the formula: $H_8[Si(Mo_2O_7)_6] \cdot 21H_2O$. The heating curve of this sample showed two endothermal effects at 112 and 150° (Fig. 3). An investigation of the character of the first process showed that at 112° the heteropoly acid lost 12 molecules of water and was converted into the hydrate with composition $H_8[Si(Mo_2O_7)_6] \cdot 9H_2O$. The second endothermal effect at 150° corresponded to the moment of complete loss of water of crystallization of silicomolybdic acid, i.e., to the formation of $H_8[Si(Mo_2O_7)_6]$; the dehydrated acid was stable and began to decompose only upon further increase in temperature; complete decomposition of the heteropoly acid was complete at about 420° when the sum of oxides $SiO_2 \cdot 12MoO_3$ formed.

The silicotungstic acid which we used for thermographic investigation corresponded to the hydrate with 18 water molecules: $H_8[Si(W_2O_7)_6] \cdot 18H_2O$. The thermogram of silicotungstic acid showed two endothermal effects at 125 and 280°; further heating did not result in any well-defined thermal effects on the heating curve (Fig. 4).

A study of the character of the dehydration processes of silicotungstic acid showed that the endothermal effect, noted at 125°, corresponded to a loss of 14 molecules of water by the heteropoly acid; therefore, at this temperature the crystal hydrate of composition $H_8[Si(W_2O_7)_6] \cdot 4H_2O$ formed. The second endothermal effect at 280° corresponded to the complete loss of all the hydrate water by the heteropoly acid, i.e., to the formation of the compound $H_8[Si(W_2O_7)_6]$.

On further heating, the silicotungstic acid gradually decomposed and gave off water of constitution. An investigation of the solid phase, in the interval 450-480°, showed that at this temperature the heteropoly acid lost half its water of constitution and that its composition was $SiO_2 \cdot 12WO_3 \cdot 2H_2O$; at 520° the silicotungstic acid lost all water of constitution and converted to a product with the composition $SiO_2 \cdot 12WO_3$.

DISCUSSION OF RESULTS

According to the literature data, phosphomolybdic acid forms crystal hydrates of the following composition: with 12.5, 14, 16, 22, 27, 28, 29 and 30 molecules of H_2O; investigation of the binary system $H_7[P(Mo_2O_7)_6] - H_2O$ [4] by the solubility method revealed the existence of hydrates containing about 21 and 22 molecules of water; tensimetric investigations [4] revealed that hydrates also exist with 11.26, 6 and 2.6 molecules of water; thermographic investigation corroborated the existence of a hydrate with 6 molecules of H_2O and indicated the dehydration temperature of the heteropoly compound.

According to the literature data, phosphotungstic acid forms hydrates with 5.7, 14, 16.5, 19, 20, 21, 23, 24, 26, 27.5, 28, 29 and 30 molecules of water. The solubility method established the existence of hydrates containing 23.84, 26.5, 22, 16 and 11 molecules of H_2O; the tensimetric method revealed hydrates containing 21, 17, 88 and 9 molecules of H_2O.

The thermographic method led to the discovery of a new hydrate for phosphotungstic acid, which contains 4 molecules of H_2O.

According to the literature data, silicomolybdic acid forms hydrates containing 12, 13, 14, 17, 28 and 29 molecules of H_2O; the solubility method [5] revealed the existence of hydrates with 14, 15.3 and 17.8 molecules of H_2O; tensimetric investigation indicated the existence of hydrates with 10.38 and 5 molecules of H_2O.

In the case of silicomolybdic acid, the record of the heating curve established the existence of another as yet unknown (in literature data) hydrate with 9 molecules of H_2O.

According to the literature data, the known hydrates of silicotungstic acid contain 5, 11, 12, 14, 15, 16.5, 17, 18, 19, 21, 22, 23, 24, 27, 30 and 31 molecules of H_2O. The thermographic method established the existence of a new, unknown in the literature, crystal hydrate with 4 molecules of H_2O. The assertion [6] was proven false that the last 2 molecules of water of constitution of silicotungstic acid are lost at 370°; we established a higher temperature for complete dehydration (520°).

The thermographic method also corroborated the isothermal investigation data on the dissociation pressure of crystal hydrates of heteropoly acids and showed that a small number of water of crystallization molecules (6 in the case of phosphomolybdic, 4 in the case of phosphotungstic and silicotungstic, 9 in the case of silicomolybdic) are bound very firmly in comparison to the other water molecules and go off at a higher temperature.

It is interesting that silicomolybdic acid and next phosphomolybdic acid contain the largest amounts of water molecules; whether or not this phenomenon is related in some way to the structural peculiarities of heteropolymolybdic acids is still unclear.

The thermographic investigation that was conducted showed very clearly that water of constitution is the most firmly bound water in heteropoly acids, the loss of which effects the decomposition of the heteropoly compound. The thermograms which we obtained convincingly showed that the heteropoly acids with phosphorus complex-formers are heptabasic and those with silicon complex-formers octabasic; thus, the thermographic investigation also confirms the high basicity of heteropoly acids as predicted by the coordination theory.

SUMMARY

1. Heating curves of phosphomolybdic, phosphotungstic, silicomolybdic and silicotungstic acids were recorded by means of N.S. Kurnakov's pyrometer.

2. It was determined by a thermographic method that water of constitution is more firmly bound than the water of crystallization and is lost at temperatures of 200-520°.

3. The quantity of water of constitution exactly corresponds to the basicity of the heteropoly acids as foreseen by the coordination theory.

4. The thermographic method established the existence of new hydrates of the heteropoly acids; a hydrate with 4 molecules of H_2O for phosphotungstic and silicotungstic acids and a hydrate with 9 molecules of H_2O for silicomolybdic acid.

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Institute of Chemical Reagents

STUDY OF CHLORINATION REACTIONS OF TITANIUM MONOXIDE

A.N. Zelikman and T. Segarchanu

Titanium tetrachloride is the basic starting material for the production of metallic titanium. In this connection, study of the chlorination conditions of various titanium compounds is of great practical importance.

The chlorination reactions of titanium dioxide with chlorine and other chlorinating agents were investigated by a number of authors [1-3]. In absence of reducing agent, the start of chlorination by chlorine with the formation of $TiCl_4$ and evolution of oxygen was observed at 800-1000°:

$$TiO_2 + 2Cl_2 = TiCl_4 + O_2. \quad (1)$$

We must take in account that the concept "temperature of the start of chlorination" is conditional. Most of the authors take for the temperature of the start of chlorination that temperature at which, during one hour, 1% of the oxide enters into the reaction.

In presence of carbon the temperature of the start of chlorination of TiO_2 decreases to approximately 350-400°, which is due to the binding of oxygen in oxides of carbon:

$$TiO_2 + 2Cl_2 + C = TiCl_4 + CO_2, \quad (2)$$

$$TiO_2 + 2Cl_2 + 2C = TiCl_4 + 2CO. \quad (3)$$

The chlorination conditions of the lower oxides of titanium (Ti_2O_3, TiO) were not investigated. There recently appeared mention that the lower oxides chlorinate at a lower temperature than TiO_2 [4].

The interaction between chlorine and titanium monoxide might be theoretically supposed to go according to the following two reactions:

$$TiO + 2Cl_2 = TiCl_4 + \tfrac{1}{2}O_2, \quad (4)$$

$$2TiO + 2Cl_2 = TiCl_4 + TiO_2. \quad (5)$$

In presence of carbon chlorination may proceed by reactions:

$$TiO + 2Cl_2 + C = TiCl_4 + CO, \quad (6)$$

$$2TiO + 4Cl_2 + C = 2TiCl_4 + CO_2. \quad (7)$$

Using the available data on the heat capacities, entropy values and heat contents of the compounds that participate in the discussed reactions (1-7) we calculated the changes of the free energy as a function of temperature for these reactions [6].

The dependence of ΔF on temperature in the interval 200-700° is graphically shown in Figure 1. Figure 1 shows that all the chlorination reactions of titanium dioxide with chlorine take place with a smaller change of free energy than the corresponding chlorination reaction of titanium monoxide. Of the two possible chlorination reactions of TiO in the absence of carbon, Reaction (5) takes place with the greater change of ΔF.

Thus, it follows from the thermodynamic calculations that titanium monoxide should chlorinate more actively than titanium dioxide.

EXPERIMENTAL

Titanium monoxide was prepared by reduction of titanium dioxide with titanium powder [5] according to reaction: $TiO_2 + Ti = 2TiO$.

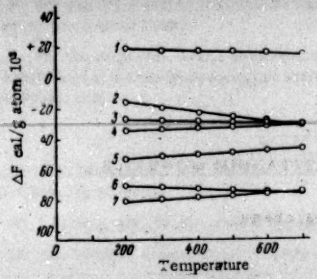

Fig. 1. Change of free energy of chlorination reactions of the monoxide and dioxide of titanium as a function of the temperature.
1) $TiO_2 + 2Cl_2 \rightarrow TiCl_4 + O_2$, 2) $TiO_2 + 2Cl_2 + C = TiCl_4 + 2CO$, 3) $TiO_2 + 2Cl_2 + C = TiCl_4 + CO_2$, 4) $TiO + 2Cl_2 = TiCl_4 + \frac{1}{2}O_2$, 5) $2TiO + 2Cl_2 = TiCl_4 + TiO_2$, 6) $TiO + 2Cl_2 + C = TiCl_4 + CO$, 7) $2TiO + 4Cl_2 + C = 2TiCl_4 + CO_2$.

Pure dioxide and metallic titanium powder were used. Their impurity content did not exceed 0.5%. Pressed cylindrical samples (from a mixture of TiO + Ti) were heated in a vacuum furnace at 1500-1600° with a pressure of $7.5 \cdot 10^{-3}$ mm Hg in the course of two hours. The scheme of the vacuum furnace is given in Figure 2. A graphite tube, held between two cooled copper electrodes, served as the heater. To avoid contact of the sample with the graphite, the sample was placed on a stand of thorium dioxide.

The obtained briquets were of a uniform yellow-bronze color along their whole cross-section. X-ray analysis of the obtained powder showed that the product had a face-centered cubic lattice (NaCl type) with parameter $a = 4.16$ A, which corresponds to the literature data for the lattice of titanium monoxide. Figure 3 shows the x-ray photograph of titanium monoxide.

Method of investigation. The chlorination study of titanium monoxide was carried out on the apparatus shown in Figure 4.

In a porcelain tube, heated by a tube electric furnace, was placed a porcelain boat with the investigated substance. For drying, the chlorine was passed through a Tishchenko bottle with sulfuric acid and a column with phosphoric anhydride. In certain experiments, moreover, the chlorine was purified from admixture of oxygen by being passed through a tube with activated carbon (heated to 700-800°). The rate of passage of the chlorine was 3.5-4 liters/hour.

Titanium chloride was collected in a flask with an outlet tube. The excess chlorine was absorbed by alkali solution.

Until the temperature of the experiment was attained, an inert gas, nitrogen or argon, was passed into the system and then chlorine was passed in. Cooling was carried out in an inert gas.

The degree of chlorination was gauged by the weight of the calcined residue after chlorination and by the quantity of $TiCl_4$ formed. For this purpose the $TiCl_4$ collected in the condensation system was subjected to hydrolysis and the quantity of TiO_2 was determined gravimetrically.

Experimental Results and Discussion.

The chlorination experiments were carried out at a temperature from 300 to 700°. The object of the study was the degree of chlorination of the pure TiO and TiO in mixture with carbon, the quantity of which was taken from calculation according to Reaction (6)*. The duration of the experiment was one hour. For comparison of the ease of chlorination of TiO and TiO_2 we carried out several chlorination experiments with titanium dioxide in presence of carbon. A stoichiometric quantity of carbon was taken according to Reaction (3) (Table 1-3, Figure 5).

The degree of chlorination, calculated by the weight of the calcined residue, was in all cases higher than that calculated by the condensed $TiCl_4$. The first value is more

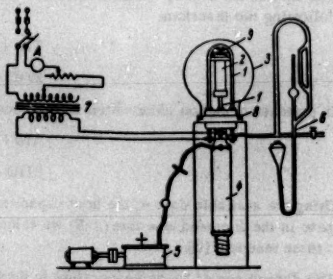

Fig. 2. Scheme of vacuum furnace. 1) Water-cooled current-lead tubes; 2) graphite heater; 3) vacuum chamber; 4) diffusion pump; 5) prevacuum pump; 6) McLeod manometer; 7) transformer; 8) vacuum seal, 9) clamp spring.

*We used calcined lamp black with an ash content no higher than 0.04%.

accurate, since losses occurred during collection and also during hydrolysis.

The experiments showed that chlorination of TiO with chlorine proceeds at a considerable rate even at 300° while the start of chlorination of TiO_2 with chlorine is above 800°. At temperatures of 400-700° the degree of chlorination of TiO does not depend on the temperature and is 40-50%. It follows from this that chlorination of titanium monoxide with chlorine takes place in this temperature interval according to the reaction:

$$2TiO + 2Cl_2 = TiCl_4 + TiO_2,$$

which agrees with the conclusions reached from thermodynamic calculation.

After 50% of the titanium monoxide reacts, only titanium dioxide remains in the boat, the marked chlorination of which takes place only above 800°. In presence of carbon the degree of chlorination of TiO reaches 97% at 500°, while under the same conditions, TiO_2 is chlorinated to no greater extent than 50%. Since upon chlorination of TiO there forms TiO_2, a smaller difference in the degree of chlorination of TiO and TiO_2 in mixture with carbon might have been expected. However, it must be noted that the titanium dioxide that forms upon chlorination of TiO must be more active, since the reaction with carbon and chlorine takes place with simultaneous rebuilding of the TiO lattice into the TiO_2 lattice. Hence, the chlorination temperature may be lowered considerably if the oxygen compound of titanium is preliminarily reduced to the titanium monoxide.

Fig. 3. X-ray photograph of titanium monoxide.

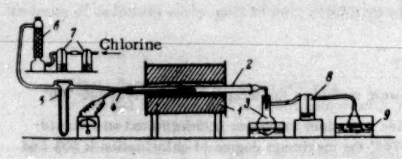

Fig. 4. Scheme of chlorination apparatus. 1) Resistance furnace; 2) porcelain tube with adapter; 3) flask with outlet tube; 4) thermocouple; 5) flow-meter; 6) column with phosphorus pentachloride; 7) Tishchenko bottle with sulfuric acid; 8) Tishchenko bottle with water, 9) vessel with alkali.

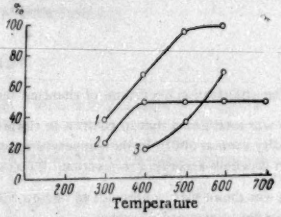

Fig. 5. Degree of chlorination of monoxide and dioxide of titanium as a function of temperature. 1) TiO + C; 2) TiO; 3) TiO_2 + C.

TABLE 1

Chlorination of TiO with Chlorine (Duration of Experiment 1 Hour)

No.	Temp.	Initial weighed sample TiO (g)	Initial weighed sample, recalculated on TiO_2 (g)	Calcined residue after chlorination	Yield TiO_2 from $TiCl_4$ (in g)	Degree of chlorination (%) on wt. of residue	Degree of chlorination (%) on quantity of $TiCl_4$
1	300°	1.000	1.2500	0.8520	0.1940	—	15.6%
2	300	1.000	1.2500	0.8450	0.1950	—	15.8
3	300	1.000	1.3260	0.8950	0.2060	22.4	16.49
4	400	1.058	1.3240	0.6660	0.5500	49.5	41.6
5	400	1.100	1.4500	0.7153	0.6110	48.6	42.2
6	400	1.060	1.3300	0.7030	0.5600	47.5	42
7	500	1.0084	1.2600	0.6294	0.5800	50.5	46
8	500	1.0974	1.3700	0.7360	0.5740	46.2	41.9
9	600	1.0412	1.3020	0.6812	0.5617	47.1	43.1
10	600	1.0302	1.2890	0.6490	0.5356	49.7	41.6
11	700	1.0466	1.3100	0.6766	0.5800	48.4	43.35
12	700	1.0564	1.3200	0.6824	0.5922	48.3	44.9

TABLE 2

Chlorination of TiO in Presence of Carbon (Duration of Experiment 1 Hour)

No.	Temp.	Weighed sample of mixture TiO + C (g)	TiO in mixture (in g)	Carbon in mixture (g)	Weight of calcined residue (g)	Obtained TiO_2 from $TiCl_4$ (g)	Degree of chlorination (%)	
							on residue	on $TiCl_4$
1	300°	1.0515	0.8770	0.1745	0.6920	0.3900	37.5	35.3
2	400	1.0120	0.8430	0.1690	0.3820	0.6650	64.8	63.0
3	400	1.1600	0.9662	0.1940	0.3924	0.6410	67.4	61.7
4	500	1.3650	1.1358	0.2278	0.0444	1.1000	97.1	89.0
5	500	1.0250	0.8548	0.1700	0.0520	0.8500	95.1	88.2
6	600	1.0777	0.8757	0.2020	0.0365	0.9450	97.0	88.0

TABLE 3

Chlorination of TiO_2 in Presence of Carbon (Duration of Experiment 1 Hour)

No.	Temp.	Weighed sample of mixture TiO_2 + 2C (in g)	TiO_2 in mixture (in g)	Carbon in mixture (g)	Weight of calcined residue after chlorination (g)	Yield TiO_2 from $TiCl_4$ (g)	Degree of chlorination (%)	
							on residue	on $TiCl_4$
1	400°	1.023	0.735	0.289	0.595	—	17.6	—
2	500	1.015	0.724	0.291	0.465	0.250	35.2	34.7
3	600	0.991	0.711	0.280	0.192	0.446	72.8	62.8

SUMMARY

1. The chlorination conditions of titanium monoxide were studied in the temperature interval 300-700°.

2. It was established that in contrast to titanium dioxide, titanium monoxide is chlorinated with considerable rapidity even at 300°. In the temperature range 400-700° the maximum degree of chlorination is 50% and chlorination proceeds according to reaction: $2TiO + 2Cl_2 = TiCl_4 + TiO_2$.

3. It was shown that in presence of carbon TiO chlorinates at 500° with considerably more rapidity than titanium dioxide in presence of carbon.

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DOUBLE DECOMPOSITION, COMPLEX-FORMATION AND POLYMORPHISM IN ADIAGONAL RECIPROCAL SYSTEM OF CHLORIDES AND SULFATES OF POTASSIUM AND CADMIUM

A.G. Bergman and E.L. Bakumskaya

Reciprocal systems of chlorides and sulfates of mono- and divalent metals offer much variety due to the abundant formation of various types of complexes between sulfates and to some degree between chlorides, and also to the very varied (in magnitude) conditional heat effects of exchange reactions. Because of this, among these reciprocal systems we find representatives of the most diverse types ranging from singular irreversible with layering – Li, Cd || Cl, SO_4 [1] through reversible-reciprocal [2] to adiagonal [3] systems in which triangulation proceeds from composition poles of the most well-defined complexes to delimiting binary systems, as shown for the system we investigated Na, Cd || Cl, SO_4 [4].

There was a clearly defined tendency of cadmium salts to autocomplex-formation as was also shown by the tendency of cadmium compounds to form complexes with salts of other metals.

TABLE 1

Binary Systems and Diagonal Sections

A) Initial component, B) added component, 1st column - mole % B, 2nd column - temperature at which first crystals appeared.

1	2	1	2	1	2	1	2	1	2	1	2
A—$CdCl_2$	B—K_2Cl_2	A—K_2Cl_2	B—K_2SO_4	A—K_2SO_4	B—$CdSO_4$	A—$CdCl_2$	B—$CdSO_4$	A—K_2Cl_2	B—$CdSO_4$	A—$CdCl_2$	B—K_2SO_4
0	568°	0	774°	0	1074°	0	568°	0	774°	0	568°
5	540	10	758	25	912	5	560	10	732	10	501
10	504	15	750	27.5	888	10	550	18	684	15	454
15	452	25	730	30	856	12.5	546	24	618	18	420
20	383	35	704	32.5	836	15	540	27	622	21	404
25	414	37.5	698	35	810	17.5	564	33	653	24	416
30	416	40	692	40	728	20	584	36	650	27	424
33	430	42.5	704	42.5	686	25	620	42	602	30	434
37.5	424	47.5	732	45	680	30	652	45	560	32.5	434
42.5	404	50	750	50	720	35	684	50	500	36	422
45	388	52.5	766	55	746			52.5	464	39.5	422
45.5	390	55	780	57.5	758			55	484	42.5	422
46	391	57.5	790	61	764			60	560	45	422
46.5	392	60	808	63	776			62.5	590	47.5	470
47	398	62.5	822	67	794			65	622	51	518
49	428	65	836	70	806			70	664	55	570
51	448	67.5	850	73	814			75	696	57.5	612
52	462	70	870	76	818			80	730	60	654
55	504	72.5	886	80	822			84	778	65	724
60	570	75	902	85	900			86	832	70	780

It was characteristic that between chlorides and sulfates of the same metal there was no complex-formation with the exception of system $AgCl - Ag_2SO_4$ [5], in which the formation of two compounds was established below the eutectic line in the solid-state region.

The large number of polymorphic and homeomorphic transformations in the sulfates also indicates the internal complexity of this group of compounds. In the reciprocal system of chlorides and sulfates of potassium and cadmium which we investigated, on the crystallization surface appear fields of four complexes: $KCl \cdot CdCl_2$, $4KCl \cdot CdCl_2$, $K_2SO_4 \cdot 2CdSO_4$, $K_2SO_4 \cdot 3CdSO_4$ and also fields of polymorphic and homeomorphic transformations: $K_2SO_4 - \alpha, \beta, \gamma$-$K_2SO_4 \cdot 2CdSO_4 - \alpha$ and β.

The surface of crystallization of this system is very complex, which necessitated a large number of internal sections through the composition diagram. The general character of this system as a semireversible-reciprocal belt type was previously discussed by O.S. Dombrovskaya [6].

EXPERIMENTAL

The investigation was carried out by a visual-polythermal method in a platinum crucible in an electric furnace. The inner portion of the furnace was illuminated by a bright light bulb to permit ready viewing of the course of crystallization. The melts were vigorously stirred with a platinum stirrer. A thermocouple Pt, Rh-Au, Pd, Pt with a sensitive millivoltmeter with a mirror galvanometer was used. The salts that were used for the investigation were carefully recrystallized and dehydrated. The melts were transparent. All the compositions were given in equimolar percentages. The melting points were: K_2Cl_2 774°, K_2SO_4 1074°, $CdCl_2$ 568°, and $CdSO_4$ 1000°. At 586° a polymorphic transformation was noted for K_2SO_4 and at 856° another transformation occurred, the nature of which is as yet unclear.

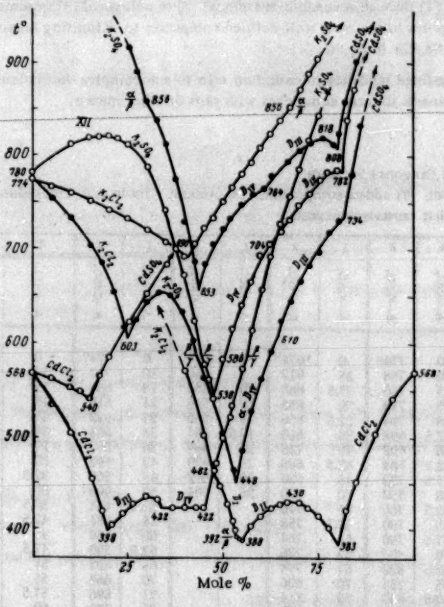

Fig. 1. Binary lateral sides, diagonal cross-sections and Section XII of reciprocal system K, Cd || Cl, SO_4.

TABLE 2. Internal Sections (Col. 1 - mole % added component; 2- temp. first crystals appeared.)

Section I		Section III		Section VI		Section VII		Section VIII		Section IX		Section XII	
1	2	1	2	1	2	1	2	1	2	1	2	1	2
0	546°	0	620°	0	766°	0	766°	0	194°	0	866°	0	780°
10	496	5	580	10	652	12.5	682	10	664	10	752	10	808
12.5	476	7.5	540	15	560	17.5	636	15	590	15	674	17.5	818
15	458	10	496	18	510	20	612	18	528	18	612	22.5	816
17.5	432	12.5	466	21	514	24	628	21	524	21	594	30	786
20	400	15	444	24	510	27	638	24	520	25	580	35	742
22.5	374	17.5	418	27	496	30	642	27	514	27.5	574	40	670
24	388	21	394	30	476	33	640	30	486	30	560	42.5	622
30	412	24	388	36	416	35	632	32	460	32.5	534	45	578
33	416	27	384	39	408	36	632	33.5	444	35	512	46	560
36	416	32.5	406	42	402	37	632	35	432	37.5	486	47.5	540
42	404	39	408	45	416	39	622	36	422	39	460	50	580
45	388	42	402	48	454	5	592	38	416	40	440	55	640
47.5	382	45	392	51	496	50	560	40	410	41	422	60	692
50	416	48	416	55	532	52.5	540	42	408	43	420	62.5	704
52.5	440	51	444	60	560	54	560	45	414	45	422	65	718
55	468	55	476	62.5	562	55	580	48	468	48	476	67.5	730
57.5	516	57.5	480	65	556	57.5	636	51	506	51	516	72.5	760
60	554	60	526	67.5	580	60	680	—	—	—	—	80	782
62.5	586	62.5	570	70	608	65	752	—	—	—	—	82.5	838
65	612	70	642	75	658	70	824	—	—	—	—	85	870

Section II		Section IV		Section XIII		Section XIV		Section XV		Section XVI		Section XVII	
1	2	1	2	1	2	1	2	1	2	1	2	1	2
0	584°	0	652°	0	440°	0	388°	0	430°	0	430°	0	430°
2	576	5	600	5	436	5	386	5	420	15	400	15	404
4	560	10	528	7.5	436	7.5	384	15	400	23	384	22.5	388
6	546	12	496	10	454	10	394	18	390	27	390	24	384
10	518	14	448	12.5	480	12.5	432	21	432	30	402	27	410
15	476	16	432	15	504	17.5	494	27	502	37	416	33	454
18	443	18	410	20	548	25	554	32.5	554	39	420	39	498
21	408	21	410	25	582	27.5	572	35	570	42	432	45	534
24	360	23	410	27.5	600	30	596	37.5	594	45	460	48	553
27	380	25	400	30	618	32.5	612	40	622	51	490	51	570
30	400	—	—	32.5	646	35	640	45	672	57	524	54	586

The conventional heat effect of the exchange reaction $K_2Cl_2 + CdSO_4 \rightleftarrows K_2SO_4 + CdCl_2$ was equal to 2.17 kcal/equiv. in the direction of the pair (left to right) K_2SO_4 and $CdCl_2$, which, however, did not constitute a stable diagonal cross-section. As we show in what follows, the system is related to the adiagonal belt type.

Binary systems (Fig. 1, Table 1). 1) $K_2Cl_2 - K_2SO_4$ [7]. The eutectic was at 690° and 41% K_2SO_4. On the K_2SO_4 branch we detected a transformation at 856° and 68.5% K_2SO_4. 2) $CdCl_2 - CdSO_4$ [8]. The eutectic was at 540° and 15% $CdSO_4$. The fusion curve was investigated up to 35% $CdSO_4$ due to the great volatility of $CdCl_2$ at high temperatures. 3) $K_2Cl_2 - CdCl_2$ [9]. According to our data, two complexes formed: $KCl \cdot CdCl_2$ with a clear maximum at 430° and 33% K_2Cl_2 and $4KCl \cdot CdCl_2$, which melted with decomposition at the transition point 462° and 52% K_2Cl_2. On the branch of this compound a transformation appeared at 392° and 46.5% K_2Cl_2. The fusion curve showed two eutectic points: 383° and 20%, 388° and 45% K_2Cl_2. 4) $K_2SO_4 - CdSO_4$ [10]. Our investigations confirmed the formation of two complexes in the system: $K_2SO_4 \cdot 2CdSO_4$ which melted with decomposition at the transition point 764° and 60.5% $CdSO_4$ and $K_2SO_4 \cdot 3CdSO_4$, which showed a clear maximum at 818° and 75% $CdSO_4$. On the K_2SO_4 branch a transformation was detected at 856° and 29.5% $CdSO_4$. There was a eutectic at 653° and 43.5% $CdSO_4$.

Diagonal cross-sections (Fig. 1, Table 1). 1) Unstable cross-section $K_2Cl_2 - CdSO_4$. The five main branches of crystallization K_2Cl_2, K_2SO_4, D_{IV}, D_{III}, $CdSO_4$ intersect at 603° and 20%, 448° and 53%, 610° and 64.5%, 740° and 81.5% $CdSO_4$.* On the K_2SO_4 branch, the curves of the β- and γ-modifications intersect at 586° and 43% $CdSO_4$. 2) Unstable cross-section $CdCl_2 - K_2SO_4$. The four main branches of crystallization $CdCl_2$, D_{III}, D_{IV},

*To save space, the following abbreviations are used: D_I - $4KCl \cdot CdCl_2$, D_{II} - $KCl \cdot CdCl_2$, D_{III} - $K_2SO_4 \cdot 3CdSO_4$, D_{IV} - $K_2SO_4 \cdot 2CdSO_4$.

TABLE 3

Composite

Sect. No.	Initial Mixture of Components	Melting point of initial mixture	Added component	Branches of curves of crystallization and their intersections																			
				Branch I	I and II		Branch II	II . III		Branch III	III . IV		Branch IV	III . IV		Branch V	V . VI		Branch VI
					% *	t		%	t		%	t		%	t		%	t	
I	8.75% $CdCl_2$ + 91.25% $CdSO_4$	546°	K_2Cl_2	$CdCl_2$	21.5	370°	D_{II}	47	376°	D_I	54.5	458°	K_2Cl_2									
II	80% $CdCl_2$ + 20% $CdSO_4$	584	K_2Cl_2		6	528		23.5	360	D_{II}												
III	75% $CdCl_2$ + 25% $CdSO_4$	620	K_2Cl_2		10	484	$CdCl_2$	20	398													
IV	70% $CdCl_2$ + 30% $CdSO_4$	652	K_2Cl_2		13.5	452		17.5	410	D_{III}	25	370	D_I	47	384°	γ-K_2SO_4	58.5	482°	K_2Cl_2
V	57.5% $CdCl_2$ + 42.5% $CdSO_4$	[724] **	K_2Cl_2		17	480		38.5	402	β-D_{IV}	42.5	386										
VI	50% $CdCl_2$ + 50% $CdSO_4$	[766]	K_2Cl_2	$CdSO_4$	17.5	506		33.5	422		43	396	γ-K_2SO_4	65.5	550	K_2Cl_2			
VII	50% $CdCl_2$ + 50% $CdSO_4$	[766]	K_2SO_4		18	602	D_{III}	35.5	630		52.5	536		55.5	586	β-K_2SO_4			
VIII	45% $CdCl_2$ + 55% $CdSO_4$	[794]	K_2Cl_2		17.5	528		33	446	α-D_{IV}	35.5	422										
IX	30% $CdCl_2$ + 70% $CdSO_4$	[866]	K_2Cl_2		18	596		34	514		41	422	β-D_{IV}	43.5	400	γ-K_2SO_4			
X	50% K_2SO_4 + 50% $CdSO_4$	720	K_2Cl_2	α-D_{IV}	10	598	β-K_2SO_4	69	640	K_2Cl_2				44.5	415				
XI	65% K_2SO_4 + 35% $CdSO_4$	810	K_2Cl_2	β-K_2SO_4	66	664	K_2Cl_2												
XII	55% K_2SO_4 + 45% K_2Cl_2	780	$CdSO_4$		44.5	586	γ-K_2SO_4	47.5	536	α-D_{IV}	62.5	704	D_{III}	81.5	782				
XIII	50% K_2Cl_2 + 50% $CdCl_2$	440	K_2SO_4																
XIV	45% K_2Cl_2 + 55% $CdCl_2$	388	K_2SO_4	D_I	9	436		25.5	586	β-K_2SO_4									
XV	33% K_2Cl_2 + 67% $CdCl_2$	430	K_2SO_4		9.5	380													
XVI	33% K_2Cl_2 + 67% $CdCl_2$	430	50% K_2SO_4		18	390	γ-K_2SO_4	36.5	586	β-K_2SO_4									
			50% $CdSO_4$		25	376	β-D_{IV}	40	422	α-D_{IV}									
XVII	33% K_2Cl_2 + 67% $CdCl_2$	430	25% K_2SO_4	D_{II}	24.5	382													
			75% $CdSO_4$				D_{III}												
XVIII	33% K_2Cl_2 + 67% $CdCl_2$	430	$CdSO_4$		20	374		46	530	$CdSO_4$									

* Percentage of added component.

** The bracketed temperatures were found by interpolation.

TABLE 4

Temperature and Composition of Invariant Points

Character of point	Temp	Composition (mole %)			Equilibrium phases
		K_2Cl_2	$CdSO_4$	$CdCl_2$	
Transitional	454°	56.5	8.5	35	K_2Cl_2, $4KCl \cdot CdCl_2$, γ-K_2SO_4
Eutectic	354	48	9.5	42.5	$4KCl \cdot CdCl_2$, $KCl \cdot CdCl_2$, γ-K_2SO_4
Eutectic	370	42	22.5	35.5	$KCl \cdot CdCl_2$, β-K_2SO_4 · $2CdSO_4$, γ-K_2SO_4
Transitional	380	33.5	26.5	40	$KCl \cdot CdCl_2$, $K_2SO_4 \cdot 3CdSO_4$, β-$K_2SO_4 \cdot 2CdSO_4$
Eutectic	352	24	17	59	$KCl \cdot CdCl_2$, $K_2SO_4 \cdot 3CdSO_4$, $CdCl_2$
Transitional	423	15.5	29	55.5	$CdCl_2$, $K_2SO_4 \cdot 3CdSO_4$, $CdSO_4$

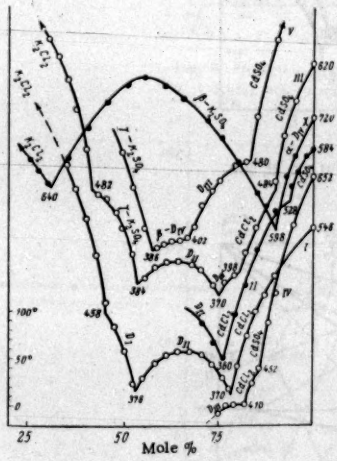

Fig. 2. Internal sections of Systems I, II, III, IV, V, X.

K_2SO_4 intersect at 398° and 20%, 422° and 33.5%, 422° and 45% K_2SO_4. On the K_2SO_4 branch intersection of the curves of the β- and γ-modifications takes place at 586° and 56% K_2SO_4.

Reciprocal system. 18 internal sections* (Figures 1-3, Table 2) were investigated. Composite Table 3 gives the compositions of the cut intersections and their temperatures. The surface of crystallization of the system (Figure 4 and 5) consists of 8 main fields of crystallization, of which 4 belong to complexes.

In the field of K_2SO_4, represented by a relatively large area, sections of the α-, β- and γ-modifications appear. The size of the fields in percent of the area of the square: K_2Cl_2 11.69, K_2SO_4 39.34 (α 8.06, β 22.9, γ 8.38), $CdCl_2$ 4.56, $CdSO_4$ 14.09, $4KCl \cdot CdCl_2$ 0.68, $KCl \cdot CdCl_2$ 5.47, $K_2SO_4 \cdot 3CdSO_4$ 13.78, $K_2SO_4 \cdot 2CdSO_4$ 10.39, (α 9.02, β 1.37).

The fields of K_2SO_4 and $KCl \cdot CdCl_2$ show crests which tend toward the sides opposite to the stable triangulating cross-section $KCl \cdot CdCl_2 - K_2SO_4$. The fields of the chloride complexes are strongly compressed by the fields of sulfate complexes. It must be noted, however, that complex $KCl \cdot CdCl_2$ also maintains the congruent character of its melting in the system as does complex $K_2SO_4 \cdot 3CdSO_4$. The figurative point of composition $KCl \cdot CdCl_2$ is the main triangulation pole.

From it extend three triangulating secants, two of which have the character of binary systems and pass through eutectic points e_I and e_{II} at 390 and 382°.

The sulfate-complex fields occupy long extended areas. At 422° polymorphism is detected in the field of complex $K_2SO_4 \cdot 2CdSO_4$. The isotherm which passes along a small portion of diagonal $CdCl_2 - K_2SO_4$ serves as

*To save space, we omitted certain sections and a number of points in the tables.

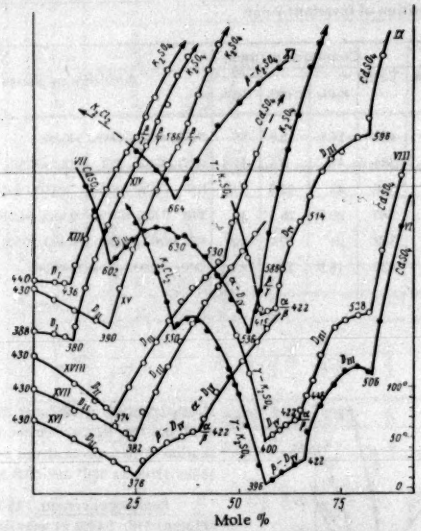

Fig. 3. Internal sections of Systems VI, IX, XI, XIII, XIV-XVIII.

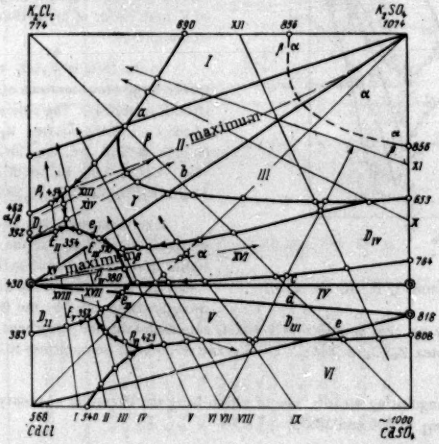

Fig. 4. Arrangement of internal sections and triangulation of system K, Cd || Cl, SO_4. Explanation in text.

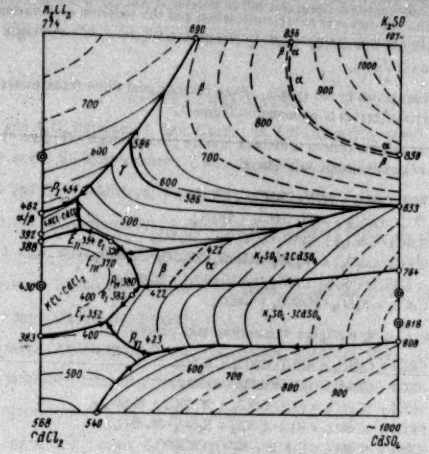

Fig. 5. Projection of space diagram of reciprocal system K, Cd ‖ Cl, SO_4 on square of composition.

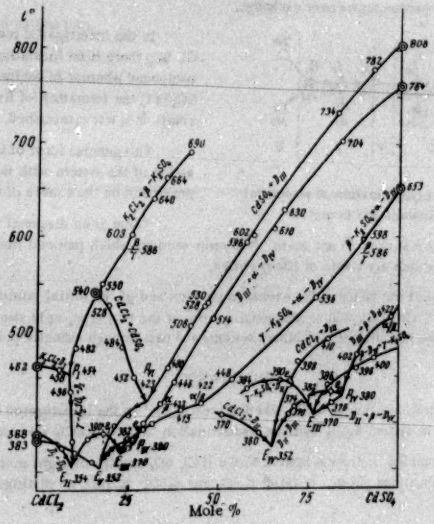

Fig. 6. Projection of curves of co-crystallization on plane of polytherm of binary system $CdCl_2 - CdSO_4$. Explanation in text.

the boundary of the α- and β-forms (the phases of these modifications are sharply distinct from each other).

To accurately determine the curves of co-crystallization and the location of invariant points, two projections were made, one of which, on side $CdCl_2 - CdSO_4$, is shown in Figure 6. To the right on this figure an enlarged detail of the projection is shown.

There are six non-variant points in the system: three eutectic and three transitional (Figures 4, 5, Table 4). The scheme of the tree of crystallization is presented in Figure 7.

By five triangulating secants the system is divided into six phase triangles (Figure 4) in which complex reactions of complex-formation and exchange take place:

1. $7KCl + CdSO_4 = 4KCl \cdot CdCl_2 + KCl + K_2SO_4$,
2. $9KCl + 2CdSO_4 = 4KCl \cdot CdCl_2 + KCl \cdot CdCl_2 + 2K_2SO_4$,
3. $9KCl + 5CdSO_4 = 3[KCl \cdot CdCl_2] + K_2SO_4 \cdot 2CdSO_4 + 2K_2SO_4$,
4. $6KCl + 7CdSO_4 = 2[KCl \cdot CdCl_2] + [K_2SO_4 \cdot 2CdSO_4] + K_2SO_4 \cdot 3CdSO_4$,
5. $12KCl + 20CdSO_4 = 2[KCl \cdot CdCl_2] + 5[K_2SO_4 \cdot 3CdSO_4] + 3CdCl_2$,
6. $2KCl + 5CdSO_4 = CdCl_2 + K_2SO_4 \cdot 3CdSO_4 + CdSO_4$.

At conversion points a, b, c, d, e (Figure 4) reactions take place:

(a) $6KCl + CdSO_4 = 4KCl \cdot CdCl_2 + K_2SO_4$,
(b) $3KCl + CdSO_4 = KCl \cdot CdCl_2 + K_2SO_4$,
(c) $3KCl + 3CdSO_4 = KCl \cdot CdCl_2 + 2CdSO_4 + K_2SO_4$,
(d) $3KCl + 4CdSO_4 = KCl \cdot CdCl_2 + K_2SO_4 \cdot 3CdSO_4$,
(e) $2KCl + 4CdSO_4 = CdCl_2 + K_2SO_4 \cdot 3CdSO_4$.

The studied system K, Cd || Cl, SO_4 visually reflects the interaction of exchange and complex-formation reactions. In the presence of a small conventional heat effect of 2,17 kcal/equiv. for the exchange reaction, complex-formation clearly predominates over exchange.

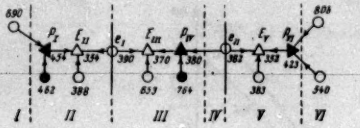

Fig. 7. Scheme of tree of crystallization of reciprocal system K, Cd || Cl, SO_4. Explanation in text.

In the investigated reciprocal system K, Cd || Cl, SO_4 there is no formation of an internal heterocompound whereas in reciprocal system K, Zn || Cl, SO_4 [11] the formation of five internal heteroionic compounds was established.

The general form of the surface of crystallization of the system with isotherms is shown in the projection on the square of composition (Figure 5).

There is no diagonal triangulation in the system, i.e., simple exchange reactions do not occur. The cross-sections which proceed from the figurative compositional points of the compounds are stable or triangulating.

These sections intersect the fields of the exchange products and of the initial components. All of the above relates reciprocal system K, Cd || Cl, SO_4 to adiagonal systems of the belt type, only two of the five triangulation cross-sections of which have the character of binary systems and pass through eutectic points e_I and e_{II}.

SUMMARY

1. An additional transformation of K_2SO_4 was detected at 856° in the investigated binary systems K_2Cl_2-K_2SO_4 and K_2SO_4-$CdSO_4$. In system K_2Cl_2-$CdCl_2$ a transformation for $4KCl \cdot CdCl_2$ was established at 392°.

2. The fusion diagram for reciprocal system K, Cd || Cl, SO_4 consists of eight main fields of crystallization which converge to six non-variant points. In fields K_2SO_4 and $K_2SO_4 \cdot 2CdSO_4$ we distinguish sections of α-, β-, γ- and α-, β-modifications.

3. The abundant complex-formation in reciprocal system K, Cd || Cl, SO_4 suppresses the exchange reaction with its small conventionally calculated heat effect of 2,17 kcal/equiv. in the direction of the pair K_2SO_4 and $CdCl_2$.

4. Reciprocal system K, Cd || Cl, SO_4 is related to the adiagonal semireversible systems of the belt type.

5. In contrast to system K, Zn || Cl, SO_4, there occurs no formation of internal heterocompounds in system K, Cd || Cl, SO_4.

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RECIPROCAL SYSTEM OF LITHIUM AND BARIUM SILICATES AND FLUORIDES

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A study of the system Li, Ba || F, SiO_3 is the result of further application of the visual-polythermal method to the study of silicate-salt and silicate systems [1,2].

The conditional heat effect of the exchange reaction in the system is equal to 3.75 kcal./equiv toward the side of the $BaF_2 - Li_2SiO_3$ pair [3].

$$\begin{array}{lcl} BaSiO_3 + 2LiF & = & BaF_2 + Li_2SiO_3 \\ 363 \text{ kcal} + 291 \text{ kcal} & & 287.9 \text{ kcal} + 374 \text{ kcal} \end{array}$$

$$\Delta = \frac{7.9}{2} = 3.95 \text{ kcal/equiv}$$

Due to the well defined tendency for complex formation the relatively small heat effect of the exchange reaction fails to synonymously determine the direction of reaction in the system. Binary and ternary complexes are formed in the system, the formation heats of which are unknown; consequently, only a study of the complete surface of crystallization elucidates the chemism of the components in the given system, which is of great interest in the systematic study of the reactions of the fluorides and silicates of lithium and of the alkali and alkaline earth metals.

EXPERIMENTAL

Method of Operation. The system was studied by the visual-polythermal method in a platinum crucible fitted with a platinum stirrer and placed in a shaft electrical furnace. A Pt-PtRh thermocouple with mirror galvanometer (with a 10 mV scale) was used to measure the temperature. A strong light beam from above served to illuminate the interior of the furnace and the melt. The liquidus curves were determined from the average temperatures of the appearance and disappearance of crystals under reduction of the intervals between them to a minimum.

The LiF and BaF_2 were prepared from c.p. carbonates and twice-distilled c.p. hydrofluoric acid, Li_2SiO_3, by the ignition, and then by the fusion in a silit furnace of c.p. lithium carbonate and silica (SiO_2). The $BaSiO_3$ was added during the process as a mixture of c.p. $BaCO_3$ and SiO_2 (ignited silicic acid). The calculations were based on equimolar percents. For brevity a part of the experimental material is not given in the tables and some of the points are omitted, but they are all shown on the curves.

Binary Systems

1. The $BaSiO_3 - Li_2SiO_3$ System (Fig. 1, Table 1) was studied by R. Wallace [4] by the method of plotting the cooling curves. He showed a eutectic at 877° and 43% Li_2SiO_3. According to our data the eutectic is found at 960° and 45%; in addition, polymorphic transformation of the Li_2SiO_3 was revealed at 986°, previously unknown.

2. The $BaSiO_3 - BaF_2$ System (Fig. 1, Table 2) was first studied from 55.0 to 67.5% BaF_2. The remaining region of the system, due to the high fusion point of $BaSiO_3$, was not studied.

A compound melting with decomposition at 1090° and having the postulated composition $2BaF_2 \cdot BaSiO_3$ was revealed (shown in Fig. 1 by the letter X). Its branch intersects with the BaF_2 branch at 65.5% BaF_2, and

TABLE 1

$BaSiO_3 - Li_2SO_3$ System

% Li_2SiO_3	Temperature	% Li_2SiO_3	Temperature	% Li_2SiO_3	Temperature
70.0	1092°	57.5	1033°	45.0	960°
67.5	1080	55.0	1017	42.5	985
65.0	1070	52.5	986	40.0	1015
62.5	1058	50.0	980	37.5	1045
60.0	1045	47.5	972	35.0	1082

TABLE 2

$BaSiO_3 - BaF_2$ System

% BaF_2	Temperature	% BaF_2	Temperature
67.5	1100°	60.0	1082°
65.0	1090	57.5	1078
62.5	1088	55.0	1100

with $BaSiO_3$ at 1075° and 58% BaF_2. Despite the small number of experimental points for this system, visually it was not difficult to show the branch belonging to this compound, since its crystals differed sharply from those of both $BaSiO_3$ (round grains) and BaF_2 (elongated prisms).

3. The $Li_2F_2 - BaF_2$ System (Fig. 1, Table 3) was studied earlier [5]. A compound melting with decomposition at 827° and having the postulated composition $LiF \cdot BaF_2$ (A) was revealed in the system. It has a very gentle crystallization branch at its intersection with the BaF_2 branch (64% BaF_2). Polymorphic transformation is revealed for BaF_2 at 920°, and homeomorphic transformation for LiF at 812°. The branches $LiF \cdot BaF_2$ and LiF intersect in the eutectic point at 760° and 32.0% BaF_2.

TABLE 3

$Li_2F_2 - BaF_2$ System

% BaF_2	Temperature	% BaF_2	Temperature	% BaF_2	Temperature	% BaF_2	Temperature
0	848°	25.0	783°	50.0	812°	75.0	916°
5.0	838	30.0	768	55.0	824	77.5	940
10.0	825	32.5	760	60.0	826	80.0	964
12.5	816	35.0	766	62.5	826	85.0	1020
15.0	810	40.0	780	65.0	837	90.0	1088
20.0	800	45.0	795	70.0	884	—	—

4. The $Li_2F_2 - Li_2SiO_3$ System (Fig. 1) has already been studied by us [1,2]. Its eutectic corresponds to 5% Li_2SiO_3 at 840°; a compound, melting with decomposition at 953° at the transition point (35% Li_2SiO_3), was revealed. Its postulated composition is $2LiF \cdot Li_2SiO_3$; polymorphic transformation on the Li_2SiO_3 branch was observed at 986°.

Diagonal Sections

1. The $Li_2F_2 - BaSiO_3$ System (Fig. 2, Table 4) was studied up to 75% $BaSiO_3$; it consists of the crystallization branches of LiF, Complex D (postulated composition $2LiF \cdot Li_2SiO_3$), Complex C (a hetero complex of postulated composition $2BaF_2 \cdot Li_2SiO_3 \cdot BaSiO_3$) and $BaSiO_3$, respectively intersecting at 827° and 6% $BaSiO_3$, 784° and 41% $BaSiO_3$, 772° and 51% $BaSiO_3$, 822° and 59.5% $BaSiO_3$.

TABLE 4

$Li_2F_2 - BaSiO_3$ Diagonal

% $BaSiO_3$	Temperature	% $BaSiO_3$	Temperature	% $BaSiO_3$	Temperature	% $BaSiO_3$	Temperature
0.0	848°	18.0	830°	42.5	784°	57.5	814°
2.0	840	21.0	828	45.0	782	60.0	827
4.0	833	24.0	826	47.5	780	65.0	908
6.0	827	30.0	816	50.0	776	67.5	950
8.0	828	35.0	802	52.5	788	70.0	992
12.5	830	40.0	788	55.0	802	75.0	1096

2. The $BaF_2 - Li_2SiO_3$ System (Fig. 2, Table 5). The fusion diagram in the studied portion (up to 82.5%

Li_2SiO_3) consists of five crystallization branches: Complex C and the α- and β- modifications of BaF_2 and Li_2SiO_3.

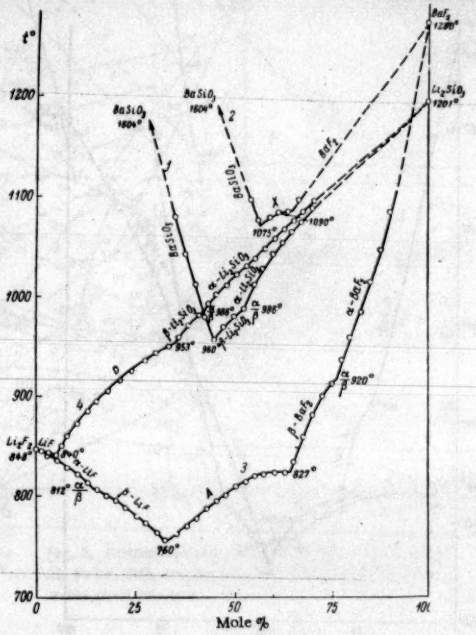

Fig. 1. Binary systems. 1) $BaSiO_3 - Li_2SiO_3$, 2) $BaSiO_3 - BaF_2$, 3) $Li_2F_2 - BaF_2$, 4) $Li_2F_2 - Li_2SiO_3$.

The branches of the α- and β-BaF_2 modifications intersect at 920° and 22% Li_2SiO_3, and α- and β-Li_2SiO_3 at 986° and 72% Li_2SiO_3. The branch of Complex C intersects with β-BaF_2 at 820° and 30% Li_2SiO_3, and with β-Li_2SiO_3 at 760° and 48.5% Li_2SiO_3.

TABLE 5

$BaF_2 - Li_2SiO_3$ Diagonal

% Li_2SiO_3	Temperature	% Li_2SiO_3	Temperature	% Li_2SiO_3	Temperature	% Li_2SiO_3	Temperature
12.5	1074°	27.5	860°	45.0	778°	67.5	955°
15.0	1036	30.0	884	47.5	764	70.0	970
17.5	990	32.5	820	50.0	781	72.5	993
20.0	950	35.0	816	55.0	836	75.0	1022
22.5	918	40.0	802	60.0	884	80.0	1066
25.0	895	42.5	792	65.0	930	82.5	1086

Internal Sections

Twenty internal sections were studied (Fig. 3, Tables 8 and 11). The first series of sections (I-V) (Fig. 4,

Tables 6 and 8) starts from the $Li_2F_2 - BaF_2$ side and goes toward Li_2SiO_3. These sections outline the LiF field, mark the boundary line between the fields of Complex D and the Li_2SiO_3 field, and also establish the boundary between the fields of Complexes D and A.

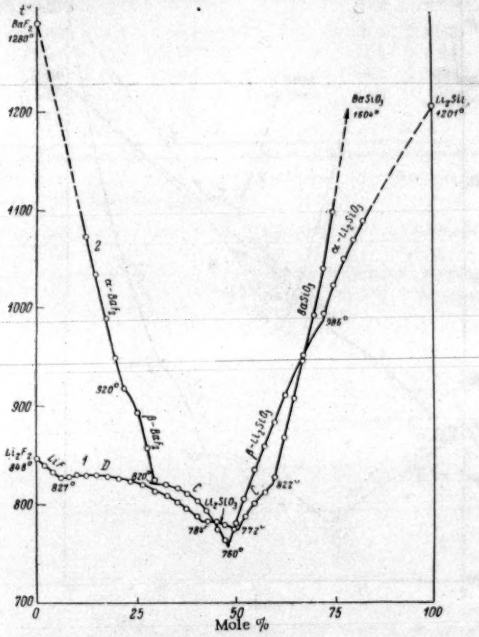

Fig. 2. Diagonal sections of the reciprocal system Li, Ba ‖ F, SiO_3.
1) $Li_2F_2 - BaSiO_3$, 2) $BaF_2 - Li_2SiO_3$.

The second series of sections (VI-XI) (Fig. 5, Tables 7 and 8) outlines the field of Compound A on the $Li_2F_2 - BaF_2$ side and two internal fields, tentatively designated as B and C. Due to the distinct crystallization and difference in the crystalline form of the phases we were able to observe even visually the transition from one field into the other. Especially noteworthy in this respect is the crystallization of Phase A, beginning with the separation of tiny point nuclei, which then grow into spherical grains. The A and B phases in sections VII, VIII and IX correspond to crystallization branches that show little difference. However, visually the crystalline forms of the two phases are easily distinguishable.

Third series of sections (XII-XV) (Fig. 6, Tables 9 and 11). All of the sections start from the $Li_2F_2 - BaF_2$ side and go toward $BaSiO_3$. These sections were studied for the purpose of elucidating the field boundaries of Compound X. The crystal form of this compound differs from that of BaF_2 and $BaSiO_3$.

Fourth series of sections (XVI-XX) (Fig. 7, Tables 10 and 11). These sections were studied for the purpose of obtaining more accurate temperatures for the boundary lines of the system, since they all go in different directions.

Projection of the three-dimensional diagram for the reciprocal system (Fig. 8). The formation of both binary complexes and ternary hetero complexes in the system was shown. Two of the eleven crystallization fields belong to two hetero complexes and three belong to side binary compounds.

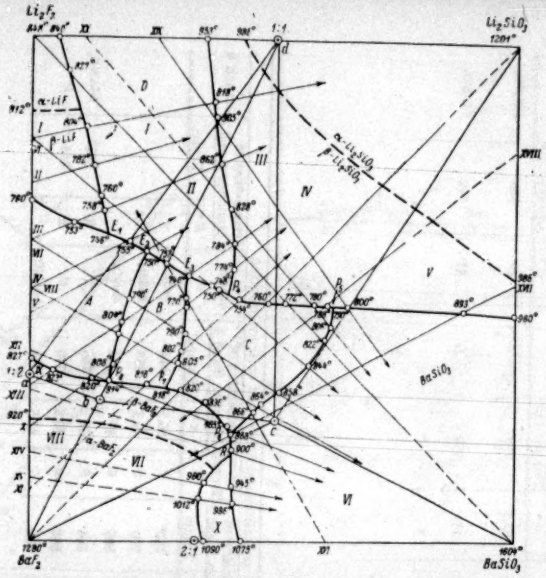

Fig. 3. Distribution scheme of the sections in the system Li, Ba || F, SiO_3 and the scheme of its triangulation into stable phase triangles.

The field areas of the eleven phases, expressed in percents of the total area of the composition square of the system, are given in Table 12. We do not subdivide the LiF field, showing homeomorphic transformation at 812°.

The projection of the points and curves on the BaF_2 – $BaSiO_3$ side is shown in Fig. 9. The ternary invariant points are characterized in Table 13. It is characteristic for the system that the maxima on the boundary lines between the eutectic points (E_1 and E_2, E_2 and E_3) exceed the temperatures of the ternary eutectic points by a total of only a few degrees; we also observe an extremely gentle descent of the boundary curves between the LiF · BaF_2 and B fields and the barium fluoride field.

Such a phenomenon can be explained by the development of complex formation in the mentioned region of the system, and also by the presumed slight difference in the heat effects for the formation of Compounds A and B. However, as was already mentioned, Phases A and B show distinct difference in their crystallization character. An analysis of the character of the whole system permits establishing the most probable compositions for the phases of the internal crystallization fields in Systems B and C. The direction of the isotherms for Fields B and C (Fig. 8) testifies to the fact that their zones are found toward the BaF_2 – $BaSiO_3$ side. However, a topological analysis of the system fails to give basis to refer the composition of these compounds to the BaF_2 – – $BaSiO_3$ side, all the more since the extremely gentle (shallow) boundary curves for Field B from the side of the BaF_2 field and for C from the side of the $BaSiO_3$ field (near point P_6) testify to their close location to the boundary lines of the zones for the compounds in Fields B and C. If the above described zone of the phases in the internal Field C is tentatively taken as corresponding to the composition 50% BaF_2, 25% Li_2SiO_3 and 25% $BaSiO_3$, then in such case the Phase C compound can be assigned the formula $2BaF_2 \cdot Li_2SiO_3 \cdot BaSiO_3$.

By analogy with the above it can be tentatively assumed that the compound in the internal Field B will

TABLE 6

First Series of Sections I-V

Section No.	Starting composition and direction of the sections	Branches of crystallization curves and their intersection									
		Branch 1	Intersection of branches 1 and 2		Branch 2	Intersection of branches 2 and 3		Branch 3	Intersection of branches 3 and 4		Branch 4
			K*	Temperature		K*	Temperature		K*	Temperature	
I	20% BaF_2 / 80% Li_2F_2 → Li_2SiO_3	LiF	10.5	804°	D	36.5	918°	β-Li_2SiO_3	49	986°	α-Li_2SiO_3
II	29% BaF_2 / 71% Li_2F_2 → Li_2SiO_3	LiF	12	782	D						
III	40% BaF_2 / 60% Li_2F_2 → Li_2SiO_3	A	8.5	753	LiF	15	758	D	37	862	β-Li_2SiO_3
IV	50% BaF_2 / 50% Li_2F_2 → Li_2SiO_3	A	19	755	D						
V	55% BaF_2 / 45% Li_2F_2 → Li_2SiO_3	A	22.5	752	D						

*K is the amount of added component in percent.

TABLE 7

Second Series of Sections VI-XI

Sect. No.	Starting composition and direction of the sections	Branches of crystallization curves and their intersection												
		Branch 1	Intersection of branches 1 and 2		Branch 2	Intersection of branches 2 and 3		Branch 3	Intersection of branches 3 and 4		Branch 4	Intersection of branches 4 and 5		Branch 5
			K*	Temp.		K*	Temp.		K*	Temp.		K*	Temp.	
VI	20% BaF_2 / 80% Li_2F_2 → $BaSiO_3$	LiF	15	760°	D	37.5	750°	C	56.5	844°	$BaSiO_3$			
VII	40% BaF_2 / 60% Li_2F_2 → $BaSiO_3$	A	19.5	790	B	31.5	790	C	49.5	858	$BaSiO_3$			
VIII	50% BaF_2 / 50% Li_2F_2 → $BaSiO_3$	A	16.5	804	B	29.5	805	C	47	864	$BaSiO_3$			
IX	69% BaF_2 / 31% Li_2F_2 → Li_2SiO_3	BaF_2	4.5	823	A	16	804	B	32	746	D	40	787°	β-Li_2SiO_3
X	77.5% BaF_2 / 22.5% Li_2F_2 → Li_2SiO_3	BaF_2	12	820	A	16	808	B	30.5	770	C	36	748	D**
XI	90% BaF_2 / 10% Li_2F_2 → Li_2SiO_3	BaF_2	23.5	816	B	31	802	C	41.5	754	β-Li_2SiO_3			

*K is the amount of added component in percent.

**Branches 5 and 6 intersect at 774°; 6 is the β-Li_2SiO_3 branch.

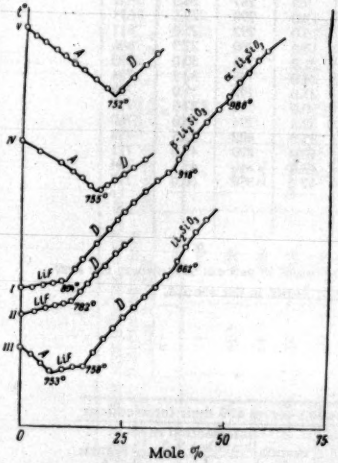

Fig. 4. First series of sections.

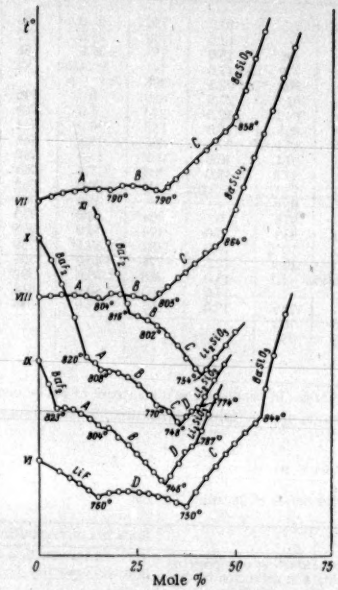

Fig. 5. Second series of sections.

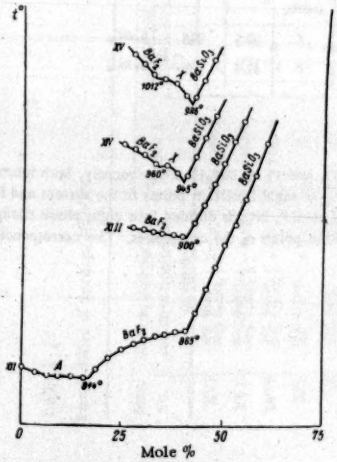

Fig. 6. Third series of sections.

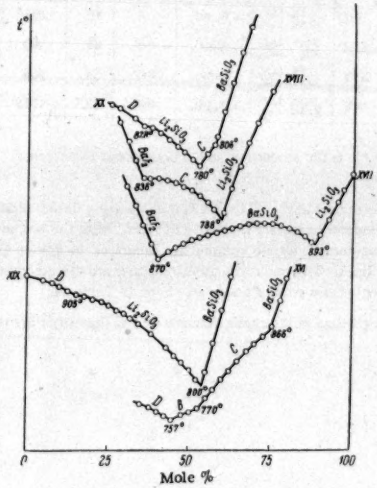

Fig. 7. Fourth series of sections.

TABLE 8

Section I		10.0	756	21.0	760	57.5	870	50.0	865
		12.5	758	25.0	772	60.0	904	52.5	892
0	796°	15.0	758	30.0	786	62.5	945	57.5	948
5.0	799	17.5	774	Section VI		Section VII		Section XI	
10.0	803	22.5	798						
12.5	815	27.5	820	0	796	0	780	15.0	912
18.0	842	32.5	840	5.0	783	6.0	786	17.5	886
24.0	868	35.0	853	10.0	774	9.0	787	20.0	856
30.0	894	37.5	866	12.5	766	12.0	790	22.5	824
35.0	914	40.0	882	15.0	760	15.0	792	25.0	811
37.5	927	45.0	908	17.5	764	18.0	790	27.5	806
40.0	939	Section IV		20.0	765	21.0	796	30.0	803
42.5	951			25.0	764	24.0	795	32.5	794
47.5	978	0	806	30.0	760	27.0	792	35.0	782
50.0	993	5.0	794	35 0	755	30.0	790	37.5	770
55.0	1015	10.0	782	37.5	750	32.5	794	40.0	760
60.0	1036	12.5	774	40.0	766	35.0	802	42.5	758
Section III		15.0	768	45.0	792	40.0	820	45.0	771
		17.0	760	50.0	814	45.0	840	47.5	784
0	778	19.0	756	55.0	838	47.5	850	50.0	797
5.0	762								
7.5	756								

Remarks: In each section the amount of added component in percent is shown in the first column, and the initial crystallization temperature is shown in the second.

TABLE 9

Third Series of Sections XII-XV

Sect. No.	Starting composition and direction of the sections	Branches of crystallization curves and their intersections						
		Branch 1	Intersection of branches 1-2		Branch 2	Intersection of branches 2-3		Branch 3
			K*	Temp.		K*	Temp.	
XII	37.5% Li_2F_2 / 62.5% BaF_2 → $BaSiO_3$	A	16	814°	BaF_2	40.5	865°	$BaSiO_3$
XIII	30% Li_2F_2 / 70% BaF_2 → $BaSiO_3$	BaF_2	41	900	$BaSiO_3$			
XIV	17.5% Li_2F_2 / 82.5% BaF_2 → $BaSiO_3$	BaF_2	34	960	X	39.5	945	$BaSiO_3$
XV	12.5% Li_2F_2 / 87.5% BaF_2 → $BaSiO_3$	BaF_2	33.5	1012	X	41.5	986	$BaSiO_3$

*K is the amount of added component in percent.

have the formula $Li_2SiO_3 \cdot 2LiF \cdot 5BaF_2$ (14.3% Li_2F_2, 14.3% Li_2SiO_3 and 71.4% BaF_2). Consequently, both internal fields correspond to ternary hetero complexes. With the presence of eight invariant points in the system and four noncleaving compounds the composition square of the system Li, Ba || F, SiO_3 is divided into eight phase triangles, shown in Fig. 3. The main triangulation zones are the composition points of the complexes. The corresponding phase triangles and ternary points are given in Table 14.

The scheme of the crystallization tree is shown in Fig. 10.

TABLE 10

Fourth Series of Sections XVI-XX

Sect. No.	Starting composition and direction of the sections	Branches of crystallization curves and their intersections									
		Branch 1	Intersection of branches 1 and 2		Branch 2	Intersection of branches 2 and 3		Branch 3	Intersection of branches 3 and 4		Branch 4
			K*	Temp.		K*	Temp.		K*	Temp.	
XVI	40% BaF_2, 60% $BaSiO_3$ → LiF_2	$BaSiO_3$	25.5	866°	C	47.5	770°	B	55	757°	D
XVII	48% $BaSiO_3$, 52% Li_2SiO_3 → BaF_2	β-Li_2SiO_3	12	893	$BaSiO_3$	60.5	870	BaF_2			
XVIII	20% $BaSiO_3$, 80% Li_2SiO_3 → BaF_2	β-Li_2SiO_3	40.5	788	C	65.5	836	BaF_2			
XIX	25% Li_2SiO_3, 75% LiF_2 → $BaSiO_3$	D	15	905	β-Li_2SiO_3	54	800	$BaSiO_3$			
XX	10% Li_2SiO_3, 90% LiF_2 → $BaSiO_3$	D	35	828	β-Li_2SiO_3	52	780	C	57	806	$BaSiO_3$

*K is the amount of added component in percent.

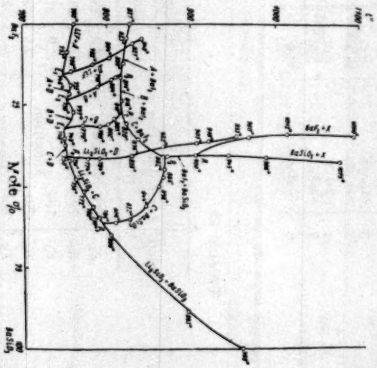

Fig. 9. Projection of the curves of joint crystallization on the BaF_2-$BaSiO_3$ side.

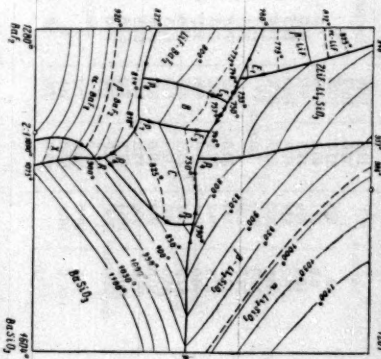

Fig. 8. Projection of the three-dimensional diagram for the reciprocal system Li, Ba || F, SiO_3.

TABLE 11

Section XII		32.5	1016
		35.0	1012
0	825	37.5	1005
6.0	817	40.0	994
12.0	816	42.5	992
15.0	814	45.0	1010
18.0	825	47.5	1030
21.0	835	Section XVI	
27.5	850		
32.5	857	20.0	928
37.5	862	22.5	902
40.0	864	25.0	870
42.5	882	27.5	857
45.0	906	32.5	836
50.0	952	40.0	806
55.0	996	45.0	782
60.0	1054	47.5	770
Section XV		50.0	766
		52.5	763
27.5	1036	55.0	757
30.0	1026	60.0	766
		65.0	776

Section XVII		10.0	914	35.0	828
		12.5	909	37.5	828
0	982	15.0	905	40.0	818
5.0	947	17.5	904	45.0	803
10.0	907	20.0	901	50.0	888
12.5	894	25.0	893	52.5	782
15.0	902	30.0	880	55.0	796
22.5	915	38.0	858	57.5	814
27.5	920	42.5	840	60.0	848
35.0	916	47.5	826	65.0	920
42.5	907	50.0	814		
50.0	894	52.5	804		
55.0	884	55.0	814		
57.5	878	57.5	850		
60.0	870	60.0	890		
62.5	894	62.5	930		
67.5	940	Section XX			
70.0	964				
Section XIX		25.0	852		
		27.5	848		
0	928	30.0	840		
5.0	924	32.5	835		

Remarks: In each section the amount of added component in percent is shown in the first column, and the initial crystallization temperature is shown in the second.

TABLE 12

Expt. No.	Crystallization field	Area (in %)	Expt. No.	Crystallization field	Area (in %)
1	LiF	4.2	7	$LiF \cdot BaF_2$	5.7
2	α-Li_2SiO_3	15.4 } 32.7	8	*B*	3.3
3	β-Li_2SiO_3	17.3 }	9	*C*	4.7
4	α-BaF_2	8.0 } 11.8	10	$2LiF \cdot Li_2SiO_4$	12.1
5	β-BaF_2	3.8 }	11	*X*	1.1
6	$BaSiO_3$	24.4			

TABLE 13

Points	Temp	Character of points	Composition (%)				Equilibrium solid phases
			Li_2F_2	Li_2SiO_3	BaF_2	$BaSiO_3$	
E_1	746°	Eutectic	45.0	13.5	39.5	—	$LiF + 2LiF \cdot Li_2SiO_4 + LiF \cdot BaF_2$
E_2	750	Likewise	34.0	23.0	43.0	—	$LiF \cdot BaF_2 + 2LiF \cdot Li_2SiO_4 + B$
E_3	746	Transition	21.0	32.0	47.0	—	$B + C + 2LiF \cdot Li_2SiO_4$
P_4	750		7.5	40.5	52.0	—	$C + Li_2SiO_4 + 2LiF \cdot Li_2SiO_4$
P_5	790	Likewise	—	52.5	39.5	8.0	$C + Li_2SiO_4 + BaSiO_3$
P_6	868	"	16.0	15.5	68.5	—	$C + BaSiO_3 + BaF_2$
P_7	818	"	3.0	27.5	69.5	—	$B + C + BaF_2$
P_8	814	"	—	21.0	60.0	19.0	$B + BaF_2 + LiF \cdot BaF_2$
R	900	Crossover	—	17.5	59.5	23.0	$X + BaF_2 + Li_2SiO_3$

TABLE 14

Triangle numbers	Triangles	Ternary point	Temp
I	Li_2F_2—LiF·BaF_2—2LiF·Li_2SiO_3	E_1	746°
II	LiF·BaF_2—B—2LiF·Li_2SiO_3	E_2	750
III	B—C—2LiF·Li_2SiO_3	E_3	746
IV	C—Li_2SiO_3—2LiF·Li_2SiO_3	P_4	750
V	C—$BaSiO_3$—Li_2SiO_3	P_5	790
VI	BaF_2—C—$BaSiO_3$	P_6	868
VII	B—C—BaF_2	P_7	818
VIII	LiF—B—BaF_2	P_8	814

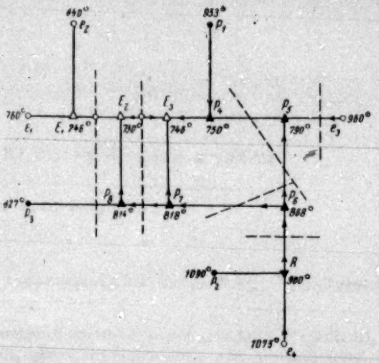

Fig. 10. Scheme of the crystallization tree for the system Li, Ba || F, SiO_3.

SUMMARY

1. The visual-polythermal method was used to study the crystallization curves of the binary systems composed of the fluorides and silicates of lithium and barium: $Li_2F_2 - Li_2SiO_3$, $BaSiO_3 - Li_2SiO_3$, $Li_2F_2 - BaF_2$, $BaSiO_3 - BaF_2$ (from 55.0 to 67.5% BaF_2) and the surface of crystallization of the ternary reciprocal system Li, Ba || F, SiO_3.

2. The surface of crystallization of the reciprocal system consists of eleven crystallization fields, three eutectics, five nonvariant transition points and one crossover point.

3. Proceeding from the character of the internal crystallization fields B and C, and also from a topological analysis of the system, it was tentatively assumed that the most probable compositions for the compounds in these fields are: $B - 2LiF \cdot Li_2SiO_3 \cdot 5BaF_2$ and $C - 2BaF_2 \cdot Li_2SiO_3 \cdot BaSiO_3$.

4. The conditional heat effect of the exchange reaction, equal to 3.75 kcal/equiv. toward the side of the $BaF_2 - Li_2SiO_3$ pair, fails to determine the direction of reaction, due to the development of complex formation in the system (both binary compounds on the side faces and also hetero complexes).

5. A study of this system by the visual-polythermal method, the same as for other systems with participation of silicate components, showed the complete possibility of studying silicate and silicate-salt systems by the simple and rapid visual-polythermal method.

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*T.p. = C.B. Translation pagination

EQUILIBRIUM DIAGRAM OF THE Na_2Cl_2–K_2Cl_2–$CaSO_4$ SYSTEM

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The system represents a stable section through the composition prism of the quaternary reciprocal system Na, K, Ca || Cl, SO_4 (Fig. 1).

Two of the side systems serve as stable diagonal sections of the two reciprocal systems Na, Ca || Cl, SO_4 [1] and K, Ca || Cl, SO_4 [2], while the third, Na_2Cl_2 – K_2Cl_2 appears as a binary system with continuous solid solutions having a minimum at 658°. Under cooling these solid solutions decompose at 500° into limited solid solutions.

The diagonal section Na_2Cl_2 – $CaSO_4$ represents a eutectic system. The diagonal section K_2Cl_2 – $CaSO_4$ appears to be more complex, since it had been established earlier [2], in contrast to the data of Janecke [3], that the heteroionic compound $CaSO_4 \cdot 2KCl$, melting with decomposition, is formed, different in its composition from anhydrokainite $KCl \cdot MgSO_4$.

EXPERIMENTAL

The studies were made by the visual-polythermal method in a platinum crucible with stirrer; an Au, Pd/Pt, Rh thermocouple and millivoltmeter with a mirror scale were used. The melting points were: KCl 770°, NaCl 800°, and $CaSO_4$, from literature data, 1450° (decomp.) ; $CaSO_4$ shows heteromorphic transformation at 1150°.

TABLE 1

Side systems						Sections					
Na_2Cl_2–$CaSO_4$		K_2Cl_2–$CaSO_4$		Na_2Cl_2–K_2Cl_2		Section I		Section II		Section III	
$CaSO_4$ (%)	Temp.	$CaSO_4$ (%)	Temp.	KCl (%)	Temp.	$CaSO_4$ (%)	Temp.	$CaSO_4$ (%)	Temp.	$CaSO_4$ (%)	Temp.
0	800°	10	739°	10	766°	0	716°	0	665°	0	658°
5	788	25	700	15	749	7.5	698	5	655	10	629
10	775	30	688	20	732	15	684	10	644	17	611
15	764	32.5	705	25	716	20	674	15	632	18	608
20	753	35	723	30	696	22.5	667	17.5	627	19	605
25	740	40	766	35	680	25	682.5	20	623	20	616
30	726	42.5	791	40	666	30	720	22.5	652	21	630
35	766	45	810	45	661	35	761	25	672	23	650
40	800	47.5	827	50	658	45	835			25	666
45	843	50	859	55	661	55	906			30	711
50	886	55	904	60	669	60	945				
55	918	60	950	65	681						

All of the data are expressed in equimolar percents. For brevity all of the experimental data are not included in the tables.

Binary Systems. The Na_2Cl_2 – K_2Cl_2 system was repeated by us (Table 1, Fig. 2). The continuous solid solutions decompose around 500°.

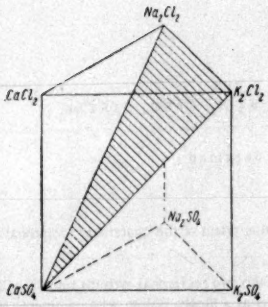

Fig. 1. The $Na_2Cl_2 - K_2Cl_2 - CaSO_4$ section in the composition prism of the system Na, K, Ca Cl, SO_4.

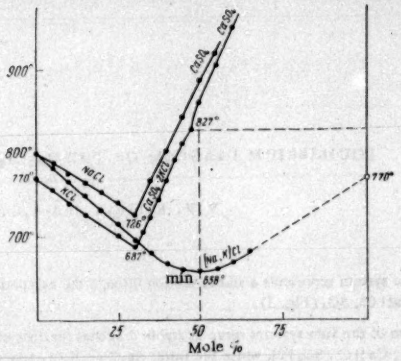

Fig. 2. Binary systems of the $Na_2Cl_2 - K_2Cl_2 - CaSO_4$ diagram.

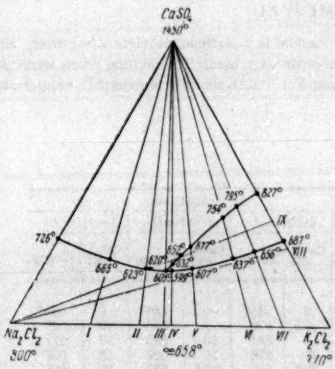

Fig. 3. Distribution scheme of the sections in the $Na_2Cl_2 - K_2Cl_2 - CaSO_4$ system.

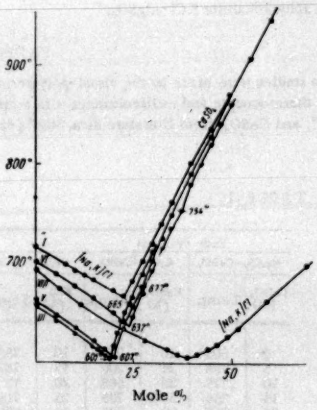

Fig. 4. Sections I, III, V, VI and VIII in the $Na_2Cl_2 - K_2Cl_2 - CaSO_4$ system.

$Na_2Cl_2 - CaSO_4$ was studied earlier [1]. It was repeated by us (Table 1, Fig. 2). The eutectic corresponds to 726° and 70% Na_2Cl_2.

$K_2Cl_2 - CaSO_4$. In the literature [3] it is indicated that only a simple eutectic exists. The system was repeated by us (Table 1, Fig. 2). The eutectic point corresponds to 687° and 30.5% $CaSO_4$, and the transition point to 827° and 47.5% $CaSO_4$.

TABLE 2

Section IV		Section V		Section VI		Section VII		Section VIII		Section XI	
$CaSO_4$ (%)	Temp	$CaSO_4$ (%)	Temp.	$CaSO_4$ (%)	Temp.	$CaSO_4$ (%)	Temp.	NaCl (%)	Temp.	NaCl (%)	Temp.
0	658°	0	663°	0	702°	0	730°	0	693°	0	743°
10	625	10	635	10	677	10	698	5.8	674	10	721
17.5	604	15	621	20	650	20	672	11.5	659	20	692
19	600	17.5	613	22.5	641	22.5	666	28	621	25	676
20	605	20	607	25	646	25	661	33.3	612	27.5	669
21	623	22.5	634	27.5	669	27.5	663	36	608	30	663
22	632	25	656	30	693	30	688	38.5	604	32.5	657
23	640	27.5	689	32.5	714	32.5	708	41	608	35	652
24	652	30	703	35	736	35	732	43.7	613	37.5	648
26	673	32.5	725	37.5	754	37.5	754	46.2	618	40	644
30	710	35	749	40	778	40	774	48.8	62.5	45	628
35	752	40	790	42.5	800	42.5	792	51.3	634	47.5	626
40	789	45	828	45	819	45	817	58.7	663	52.5	646
50	866	50	870	50	859	50	857	68.4	698	60	673

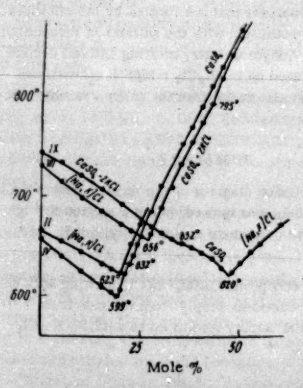

Fig. 5. Sections II, IV, VII and IX of the $Na_2Cl_2 - K_2Cl_2 - CaSO_4$ system.

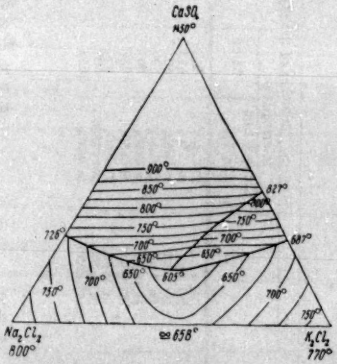

Fig. 6. Fusion diagram of the $Na_2Cl_2 - K_2Cl_2 - CaSO_4$ system.

Earlier [5,6] it was established that a compound, melting with decomposition, and having a transition point at 790° and 44.5% $CaSO_4$, is present. On the square of the reciprocal system the joint crystallization curve of the complex $CaSO_4 \cdot 2KCl$ and $CaSO_4$ has a maximum on the stable section, which gives basis to assume that this complex is a binary heteroionic compound, melting with decomposition. On the side faces in the reciprocal system there also exists a series of complexes: $KCl \cdot CaCl_2$, $K_2SO_4 \cdot 2CaSO_4$, $2K_2SO_4 \cdot 3CaSO_4$.

Ternary System. A total of 9 sections was studied (Tables 1,2,3, and Figs. 3,4,5). The study results are shown in the summary chart (Fig. 6) and on the projection of the crystallization tree (Fig. 7).

From the $K_2Cl_2 - CaSO_4$ side the field for the separation of the $CaSO_4 \cdot 2KCl$ complex extends nearly to the middle of the triangle, where it wedges into a ternary point at 605° and 38.5% K_2Cl_2, 19% $CaSO_4$ and 42.5% Na_2Cl_2. Decomposition of the solid solutions fails to be observed in the field of the $Na_2Cl_2 - K_2Cl_2$ solid solutions.

TABLE 3

Points of Intersection on the Sections

Sect. Nos.	Direction of the sections	Branches of the crystallization curves and their intersection									
		1	Composition (in %)	Temp.	2	Composition (in %)	Temp.	3	Composition (in %)	Temp.	
I	(25% K_2Cl_2+75% Na_2Cl_2) + $CaSO_4$	[Na, K]Cl	23 $CaSO_4$	665°	$CaSO_4$	—	—	—	—	—	
II	(40% K_2Cl_2+60% Na_2Cl_2) + $CaSO_4$	[Na, K]Cl	20 $CaSO_4$	623	$CaSO_4$	—	—	—	—	—	
III	(47% K_2Cl_2+53% Na_2Cl_2) + $CaSO_4$	[Na, K]Cl	19 $CaSO_4$	605	$CaSO_4$	—	—	—	—	—	
IV	(50% K_2Cl_2+50% Na_2Cl_2) + $CaSO_4$	[Na, K]Cl	19.5 $CaSO_4$	599	$CaSO_4 \cdot 2KCl$	22 $CaSO_4$	632	$CaSO_4$	—	—	
V	(57.5% K_2Cl_2+42.5% Na_2Cl_2) + $CaSO_4$	[K, Na]Cl	20 $CaSO_4$	607	$CaSO_4 \cdot 2KCl$	27 $CaSO_4$	677	$CaSO_4$	—	—	
VI	(75% K_2Cl_2+25% Na_2Cl_2) + $CaSO_4$	[K, Na]Cl	24 $CaSO_4$	637	$CaSO_4 \cdot 2KCl$	37.5 $CaSO_4$	754	$CaSO_4$	—	—	
VII	(85% K_2Cl_2+15% Na_2Cl_2) + $CaSO_4$	[K, Na]Cl	27 $CaSO_4$	656	$CaSO_4 \cdot 2KCl$	42.5 $CaSO_4$	795	$CaSO_4$	—	—	
VIII	(28% $CaSO_4$+72% K_2Cl_2) + Na_2Cl_2	[K, Na]Cl	38.5 $CaSO_4$	605	[Na, K]Cl	—	—	—	—	—	
IX	(37.5% $CaSO_4$+62.5% K_2Cl_2) + Na_2Cl_2	$CaSO_4 \cdot 2KCl$	35 Na_2Cl_2	652	$CaSO_4$	47 Na_2Cl_2	620	[Na, K]Cl	—	—	

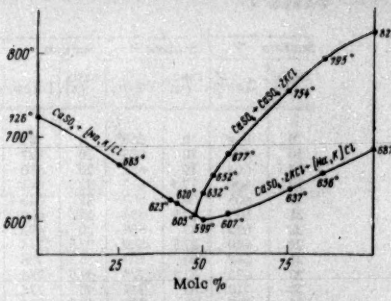

Fig. 7. Projection of the crystallization tree of the $Na_2Cl_2 - K_2Cl_2 - CaSO_4$ system. Explanation in the text.

When the earlier studied $Na_2Cl_2 - K_2Cl_2 - MgSO_4$ system [4] is compared we see considerable difference in the type of complexes that are formed by the chlorides of sodium and potassium with the sulfates of magnesium and calcium. Anhydrokainite, melting without decomposition, is formed on the $K_2Cl_2 - MgSO_4$ section, and remains as such also in the interior of the examined section.

SUMMARY

1. The fusion diagram of the ternary system $K_2Cl_2 - Na_2Cl_2 - CaSO_4$, was studied, being a section through the prism of the quaternary reciprocal system K, Na, Ca ‖ Cl, SO_4.

2. The compound $CaSO_4 \cdot 2KCl$, melting with decomposition, penetrates deeply from the side face into the region of the ternary system up to a 42.5% Na_2Cl_2 content.

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STUDY OF PHOSPHATE COMPLEXES IN SOLUTION

I. PHOSPHATE COMPLEXES OF IRON

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Phosphoric acid is often used to bind ions of trivalent iron in a colorless complex in the colorimetric determination of titanium and a number of other ions [1]. A method of colorimetrically determining phosphate was recently suggested which is based on the breaking up of thiocyanate complexes of iron by means of phosphate ions [2]. In the case of colorimetric methods of determining phosphorus, it is necessary to know the effect of other ions on the formation process of colored compounds. To solve these problems it is necessary to know the composition and stability of the metallic phosphate complexes in solution. However, as yet there is a lack of reliable data that would permit solution of problems relating to the behavior of phosphate ion in the presence of other ions.

The weakening of the coloration of ferric thiocyanate solution by the action of phosphate was known as long ago as 1875 [3]. In 1889, decolorization of iron salts under the action of phosphoric acid was observed [4]. Many investigators studied the composition of iron phosphates separated out in the solid state [5-12]. It was established that the composition of the complexes corresponded to the ratio of iron to phosphate of 1:1, 1:2 and even 1:3.

The works of L. Dede [13], which employed in a conductivity method on phosphate complexes in solution, indicate that the composition of iron-phosphate complex in solution corresponds to a ratio of phosphate to iron of 1:1. A sharp increase in conductivity upon combination of solutions of phosphoric acid and ferric chloride, in comparison to their composite conductivity, is explained by the formation of a very strong acid $H_3[FePO_4Cl_3]$. Lanford and Kiehl [14] determined the composition of iron-phosphate complex by Ostromyslensky-Zhoba's method [15,16] in which the reaction between ferric thiocyanate and phosphate ion was used. According to these data, the composition of iron-phosphate in solution corresponded to 1:1 but these data cannot be considered reliable since the formation of different iron thiocyanate complexes [2] was not taken into account. The literature [2] mentions that the composition of the complex corresponds to a ratio of iron to phosphate of 1:1 and 1:2. Polarographic investigation of solutions of ferriphosphate complexes [13] established that at a high phosphoric acid content a complex forms, the composition of which corresponds to a ratio of iron to phosphate of 1:1. From the displacement of the half-wave maximum with change in concentration of phosphoric acid, the value of the instability constant of the complex was found to be $0.7 \cdot 10^{-9}$. The composition of iron-phosphate complexes was studied [10,11,12] by means of ion exchangers; from this it was concluded that the composition of phosphate complexes depends on the ratios of the reacting components, but, in any case, corresponds to a ratio of iron to phosphate of 1:1, 1:2 and 1:3. However, a detailed investigation of these data [12] leads to another conclusion. Figure 1 shows one of the curves taken from Salmon's work [12].

The iron-phosphate complex is not very stable and thus curves $pH - \frac{[H_3PO_4]}{[FeCl_3]}$ or $\frac{\Delta[H^+]}{[Fe^{3+}]} - \frac{[H_3PO_4]}{[FeCl_3]}$ do not show sharp inflexions. Under these circumstances, it is evident that in order to find the point of inflexion corresponding to the composition of the complex, it is necessary to draw tangents to the experimental points; the point of intersection of the tangents indicates the molar ratios of acid to ferric chloride in the iron-phosphate complex. If these lines are drawn, as Figure 1 shows, the composition of iron-phosphate complex corresponds to a ratio of iron to phosphate of 2:1.

Thus, from the briefly mentioned literature survey, it is apparent that, depending on the concentrations of

the reacting components and, also, evidently, on the hydrogen ion concentration, different iron-phosphate complexes are formed in solution. All the above-described methods of determining the composition of the iron-phosphate complex in solution are indirect and are not completely reliable.

In the given communication we present experimental results on the study of the iron-phosphate complex by a direct spectrophotometric method in the ultra-violet region of the spectrum.

EXPERIMENTAL

Composition of iron-phosphate complex in solution. To determine the composition of the iron-phosphate complex, composition light-absorption diagrams in the ultra-violet region of the spectrum were studied [15,16, 17]. 0.1 M solutions of ferric perchlorate and phosphoric acid were prepared. Since the acidity of the solution may significantly affect the composition of the complex, both solutions contained an identical and considerable excess of perchloric acid. The hydrogen ion concentration in both solutions was 1 M. The measurement of light-absorption was taken on a SF-4 spectrophotometer. Figure 2 gives the absorption spectra of solutions of ferric perchlorate (Curve 1) and iron-phosphate complex (Curve 2). The wave lengths are plotted in mμ as abscissas and the molar extinction coefficients, as calculated for the iron concentration, were plotted as ordinates. Phosphoric and perchloric acids virtually do not absorb in this region. On comparing the curves, it is apparent that the iron-phosphate complex has a considerably larger molar extinction coefficient in comparison to the initial components.

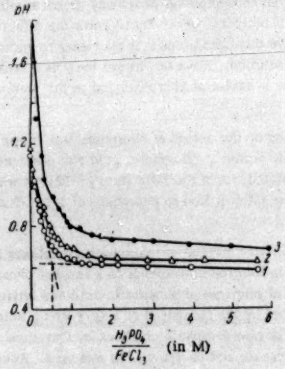

Fig. 1. Change in pH of solution upon titration of ferric chloride with phosphoric acid (Salmon's data [12]). 1) 0.1 M $FeCl_3$ + 40 g $NaNO_3$; 1.77 M H_3PO_4; 2) 0.1 M $FeCl_3$; 1.77 M H_3PO_4; 3) 0.1 M $FeCl_3$; 2.43 M H_3PO_4.

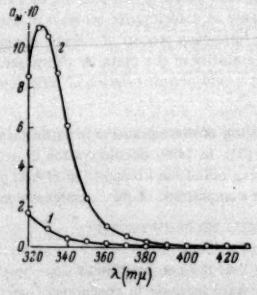

Fig. 2. Absorption spectra of solutions of ferric perchlorate (1) and iron-phosphate complex (2).

It is also evident from Figure 2 that for analysis of a composition-property diagram, light-absorption in the wave-length range of 320 to 360 mμ may be used as the property.

For the study of the composition of the phosphate complex, solutions of ferric perchlorate and phosphoric acid of the same molarity were mixed in various ratios, so that the total volume remained constant. After stirring the mixture of solutions, the optical densities for various wave lengths from 320 to 360 mμ were measured. Some experimental results on the study of the composition of the iron-phosphate complex are given in Figure 3. The ratio of the volumes of 0.1 M solutions of ferric perchlorate and phosphoric acid are plotted as abscissas and the values of the optical density of the solutions are plotted as ordinates. Curves 1 and 2 correspond to data obtained for wave lengths of 350 and 360 mμ. The experiments were carried out at an acidity of from 0.1 to 1 N for the solutions and also at concentrations of from 0.01 to 1.1 M for the reacting components. All the experiments showed that under these conditions, an iron-phosphate complex formed with a ratio of $[Fe^{3+}]:[PO_4^{3-}] = 2:1$ (Figure 3).

Determination of sign of the charge of iron-phosphate complex. To determine the sign of the charge of the iron-phosphate complex, experiments were performed to determine the direction of the migration of the complex ion during hydrolysis in a U-tube.

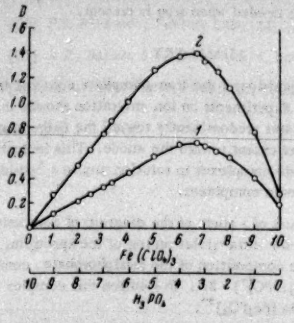

Fig. 3. Composition-optical density curves obtained by the isomolar mixture method at wave lengths of 350 and 360 mμ.

TABLE 1

Found Fe ($M \cdot 10^4$)		Found PO_4^{3-} ($M \cdot 10^4$)	
in anolyte	in catolyte	in anolyte	in catolyte
1.7	5.0	5	8
1.1	4.3	4	6
1.4	4.3	5	7
1.6	4.6	5	7

Analytical results on the catholyte and anolyte of these solutions are presented in Table 1.

The experimental results show marked migration of phosphate toward the cathode, which indicates the formation of a cationic complex. The migration of iron toward the anode was less marked; thus, under the given conditions, the formation of complex anions was noted to a considerably lesser extent.

Determination of stability of complex. The curves of Figure 3 show a diffuse maximum, which indicates the low stability of the complex which forms. To determine the stability of the complex, a method was used which was based on the study of the effect of an excess of reagent [19]. When the cited experiments were carried out, the concentration of perchloric acid was 1 M (Table 2, Figure 4).

The data of Table 2 show that practically complete binding of the iron into the phosphate complex takes place at a concentration of excess phosphoric acid equal to 1 M. Table 2 also shows the percentage of iron bound in the complex as a function of the concentration of excess phosphoric acid. These data were calculated on the basis of the obtained optical density values for the corresponding solutions. On complete binding of iron into complex, the optical density of the solution was 1.40. The optical density of free iron is disregarded in all cases, since its value is relatively small. The quantity of iron that is bound in complex is calculated from expression: $[Fe^{3+}]_{bound} = \frac{1}{2}[Fe^{3+}]_{total} \cdot \frac{Dx}{Dn}$, where D_x is the optical density of the given solution and D_n is the optical density of the solution on complete binding of iron in complex ($D_n = 1.40$). Figure 4 gives the concentration of the excess of phosphoric acid on binding of half of the iron in complex, which is $10^{-1.98}$ M $\approx 10^{-2}$ M.

TABLE 2

Concentration of excess phosphoric acid (in M)	$2.5 \cdot 10^{-3}$	$7.5 \cdot 10^{-3}$	$1.25 \cdot 10^{-2}$	$1.75 \cdot 10^{-2}$	$3.75 \cdot 10^{-2}$	$4.75 \cdot 10^{-2}$	0.5	1.0
Optical density of solution (320 mμ)	0.418	0.598	0.760	0.900	1.11	1.25	1.39	1.40
Percentage of iron bound in complex	29.0	42.6	54.3	64.3	79.3	89.3	9.3	100
$-\log C_{H_3PO_4}$	2.6	2.12	1.90	1.76	1.43	1.32	0.30	0

Thus, a cationic ferriphosphate complex forms in solution, which is characterized by low stability. Figure 5 shows than an excess concentration of 10^{-2} M phosphoric acid is necessary for binding half of the iron in complex. For complete binding of iron in complex, it is necessary to have an excess concentration of 1 M phosphoric acid; i.e., 200 times more in comparison to the iron concentration. The existence of such a complex, although of low stability, evidently is the reason why a large excess of ammonium molybdate must be added to form the phosphomolybdic heteropoly acid in the presence of iron [20]. Analysis of ferrous metals shows the content of iron to be several thousand times greater than the phosphorus content. In the case of formation of the phosphomolybdic complex in the presence of iron salts, it is necessary that the molybdate ions displace the iron from the phosphate complex and replace it. The phosphomolybdic complex is also of low stabil-

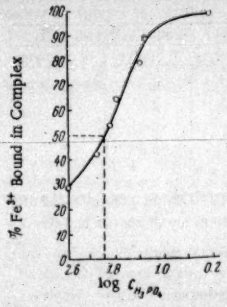

Fig. 4. Binding of iron in phosphate complex as a function of the phosphate concentration.

ity [21,22] and therefore an excess of molybdate, approximately equal to the iron, is needed when iron is present.

SUMMARY

1. The composition of the iron-phosphate complex in solution was studied. Experiments on ion migration showed that the phosphate ion migrates predominantly toward the cathode and, to a considerably lesser extent, toward the anode. This indicates the formation of cationic complexes in solution and, to a considerably lesser degree, anionic complexes.

2. On the basis of a study of the diagram of composition-light-absorption in the ultra-violet region of the spectrum, it was established that the composition of the ferriphosphate complex in solution is $[Fe^{3+}]:[PO_4^{3-}] = 2:1$. In solution this complex may be assigned the formula $[Fe_2PO_4]^{3+}$.

3. Our conclusions concerning the composition of the complex coincide with Salmon's corrected data [12], which were obtained by studying iron-phosphate complexes by means of adsorbents.

4. To bind half of the iron in complex it is necessary to have an excess concentration of $1.05 \cdot 10^{-2}$ M phosphate ion. This value characterized the stability of the ferri-phosphate complex of iron.

5. The formation of the iron-phosphate complex explains the necessity of using a large excess of molybdate in determining phosphorus in ferrous metals.

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OXALATE COMPLEXES OF IRON (III)

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The existence of oxalate complexes of iron (III) and iron (II) was noted even in the works of Eder and Valenta [1]. These compounds were studied in greater detail by Schaffer and Abegg [2], who considered them to be salts of ferri- and ferrooxalic acids $Me_3[Fe(C_2O_4)_3]$ and $Me_2[Fe(C_2O_4)_2]$. Further investigation of the stability of iron-oxalate complexes was undertaken by V.F. Toropova [3]. She determined, by a polarographic method, the dissociation constant of the iron-ferrooxalate complex, on the basis of which she calculated the dissociation constant of the ferrioxalate complex:

$$K_{Fe(C_2O_4)_3^{3-}} = \frac{[Fe^{3+}][C_2O_4^{2-}]^3}{[Fe(C_2O_4)_3^{3-}]} = 1.2 \cdot 10^{-24}.$$

However, in calculating this and other magnitudes, it was accepted that the concentration of $C_2O_4^{2-}$ ion corresponded to the total concentration of $H_2C_2O_4$. However, oxalic acid is a weak acid, and, therefore, without data on the pH of the solution, it is not possible to calculate the free oxalate ion concentration.

On studying the heats of formation of complex compounds of divalent metals (Mn, Co, Ni, Cu, Zn) with oxalate ion, K.B. Yatsimirsky and E.K. Zolotarev [4] by interpolation, calculated the reaction heat of formation of $Fe(C_2O_4)_2^{2-}$ and then the instability constant of this ion. Further, using the data of V.F. Toropova, according to which $\frac{K_{Fe(C_2O_4)_3^{3-}}}{K_{Fe(C_2O_4)_2^{2-}}} = 4.5 \cdot 10^{-15}$, and value of $K_{Fe(C_2O_4)_2^{2-}}$, which was found by interpolation, the authors calculated $K_{Fe(C_2O_4)_3^{3-}}$. It proved equal to $3.7 \cdot 10^{-21}$.

Lambling [5], on the basis of neutralization curves of solutions of trivalent iron which contained various quantities of oxalate ion, demonstrated the presence of the following equilibria in the system.

$$Fe^{3+} + C_2O_4^{2-} = FeC_2O_4^{+} \quad (1)$$

$$FeC_2O_4^{+} + C_2O_4^{2-} = Fe(C_2O_4)_2^{-} \quad (2)$$

$$Fe(C_2O_4)_2^{-} + C_2O_4^{2-} = Fe(C_2O_4)_3^{3-} \quad (3)$$

The corresponding dissociation constants were also determined: $K_1 = 10^{-9.4}$, $K_2 = 10^{-6.8}$, $K_3 = 10^{-4}$. However, in calculating the values of the constants, the dependence of the free oxalate ion concentration on the pH of the solution was not taken into account. Moreover, in calculating the constants, the effect of pH with respect to shifting the equilibria of complex-formation was not considered. In this connection, the conclusions contradict the experimental conditions. Thus, for example, from the expression of the second instability constant can be calculated the free oxalate ion concentration at which the half the quantity (or more) of the first complex group is converted to the second in accord with Equation (2):

$$K_2 = \frac{[FeC_2O_4^{+}][C_2O_4^{2-}]}{[Fe(C_2O_4)_2^{-}]} = 10^{-6.8}, \text{ in which } [Fe(C_2O_4)_2^{-}] > [FeC_2O_4^{+}]$$

if

$$[C_2O_4^{2-}] \geq 10^{-6.8}. \quad (4)$$

The acid dissociation constant of oxalic acid is equal to:

$$K = \frac{[H^+]^2[C_2O_4^{2-}]}{[H_2C_2O_4]} = K_1K_2 = 10^{-5.2} \qquad (5)$$

In Lambling's work, a (total) concentration of the order of 10^{-3}M oxalate and more was used. Thus, Condition (4) is fulfilled at a H^+-ion concentration of $[H^+] = \sqrt{\frac{10^{-5.2} \cdot 10^{-3}}{10^{-6.8}}} = \sqrt{10^{-1.4}} = 10^{-0.7}$.

Consequently, in accord with Lambling's data on the instability constant, at pH > 0.7 a large portion of the iron goes from complex $FeC_2O_4^+$ to complex $Fe(C_2O_4)_2^-$. Lambling calculated the value of the constant for complex $FeC_2O_4^+$ at pH 3 and higher.

In the present work an attempt was made to investigate complex-formation in system $Fe^{3+} - C_2O_4^{2-}$ by using physicochemical analytical methods.

Determination of the composition of complexes by equilibrium with colored ferric complexes in isomolar series. The method was similar to that used for investigating colored complexes of ferric fluoride by equilibrium with a colored ferric thiocyanate complex [6]. As a property of the investigated system $Fe^{3+} - C_2O_4^{2-} - SCN^-$ the optical density of the solutions was measured. The ratios of the volumes of Fe^{3+} (with addition of potassium thiocyanate) and oxalate solutions were plotted as abscissas; in the series of solutions the sum of the gram-ion concentrations of iron (III) and oxalate remained constant. The decrease in the intensity of the color, caused by formation of the colorless oxalate complex, was plotted as ordinates. The reaction was carried out at pH ≈ ≈ 1-2 (to avoid hydrolysis of ferric salts), at which the concentration of oxalate ion is strongly reduced due to binding in the $H_2C_2O_4$ molecule. At a thiocyanate concentration of $[SCN^-] \approx K_{FeSCN^{2+}}$ iron is present chiefly in the form of the complex monothiocyanate cation.

Thus, the equilibrium we studied may be represented by the following equation:

$$FeSCN^{2+} + nC_2O_4^{2-} = Fe(C_2O_4)_n^{(2-2n)} + SCN^-.$$

Two series of experiments were carried out to determine the composition. As the first component of the first series a solution was taken which contained $8 \cdot 10^{-4}$ mole ferric nitrate and $8 \cdot 10^{-3}$ mole potassium thiocyanate in 1 liter. The second component was an $8 \cdot 10^{-4}$M solution of ammonium oxalate. All solutions contained 0.05 mole nitric acid in 1 liter. The measurements of optical density were carried out on a PM photometer at an effective wave length of 465 mμ and a layer thickness of 10 mm. The results of the measurements are given in Table 1.

TABLE 1

Volume of solution (ml)		Optical density		
$FeSCN^{2+}$	$(NH_4)_2C_2O_4$	in presence of $(NH_4)_2C_2O_4$	without $(NH_4)_2C_2O_4$	$\bar{D}$
8	2	1.43	1.65	0.22
7	3	1.08	1.45	0.37
6	4	0.68	1.22	0.54
5	5	0.31	1.01	0.70
4	6	0.13	0.76	0.63
3	7	0.05	0.50	0.45
2	8	0.03	0.29	0.26

Column 4 of Table 1 gives the results of measuring the optical density of solutions of the second series, which were prepared the same as solutions of the first series (Column 3), only without oxalate ion; in its place was added corresponding amounts of 0.05 N nitric acid. Column 5 gives the values for the decrease in optical density ($\bar{D}$) of ferric thiocyanate due to formation of ferric oxalate.

Figure 1 presents a diagram of the properties of system $FeSCN^{2+} - H_2C_2O_4$ in accordance with the data of Table 1. Curve 1 shows the optical density of solutions of the first series, Curve 2 – the optical density of solutions of control experiments. The difference in the optical density values of the solutions, i.e., decrease in optical density caused by complex-formation, is shown in the same scale by Curve 3.

The maximum decolorization was observed at a ratio of $Fe^{3+} : C_2O_4^{2-} = 1:1$. Under the given conditions,

this indicates the formation of a complex, the composition of which, evidently, corresponds to the formula $FeC_2O_4^+$.

The formation of a similar complex was confirmed also by a series of experiments using the isomolar-series method for system $Fe^{3+} - H_2Sal - C_2O_4^{2-} - H_2O$. With salicylic acid in acid medium (pH up to 2) the trivalent iron forms a red-violet complex cation $\left[C_6H_4\begin{smallmatrix}O\\COO\end{smallmatrix}Fe\right]^+$ [7]. A solution containing ferric nitrate ($4 \cdot 10^{-3}$ M) and salicylic acid ($4 \cdot 10^{-3}$ M) was taken as the first component and ammonium oxalate ($4 \cdot 10^{-3}$ M) was taken as the second component of the series. The concentration of nitric acid in all solutions was 0,1 N. The results of measuring the optical density at 533 mμ are given in Table 2.

TABLE 2

Volume of solutions (in ml)		Optical density		
$FeSal^+$	$(NH_4)_2C_2O_4$	without $(NH_4)_2C_2O_4$	in presence of $(NH_4)_2C_2O_4$	$\bar{D}$
8	2	1,37	1,15	0.22
7	3	1,16	0,77	0,39
6	4	0,91	0,39	0,52
5	5	0,68	0,09	0,59
4,5	5,5	0,57	0,01	0,56
4	6	0,45	0,01	0,44
3	7	0,26	0	0,26
2	8	0,06	0	0,06

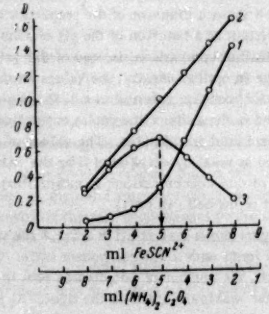

Fig. 1. Isomolar series of system $FeSCN^{2+} - (NH_4)_2C_2O_4$. Explanation in text.

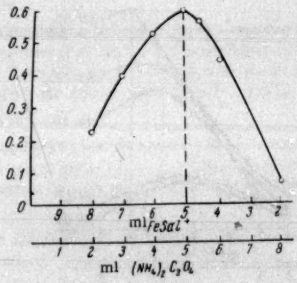

Fig. 2. Isomolar series of system $FeSal^+ - (NH_4)_2C_2O_4$.

Figure 2, plotted in coordinates (composition of complex-decrease in optical density) shows that the maximum decolorization, i.e., the formation of the iron-oxalate complex is observed at a ratio of Fe^{3+} and $C_2O_4^{2-}$, of 1:1. On increasing the concentration of oxalate ion, the formation of other complexes, aside from the simple $FeC_2O_4^+$ complex, with a larger number of coordinated oxalate ions, is to be expected. Therefore, the section of system $Fe^{3+} - C_2O_4^{2-}$ - solvent, which corresponds to the isomolar series, depending on the $[C_2O_4^{2-}]$ concentration, may pass through fields in which other complexes predominate [8].

Increase in the oxalate ion concentration may be accomplished by increasing the pH of the solution; we therefore studied isomolar series of the system ferric monosalicylate-oxalic acid at various pH values of solution.

A solution of ferric monosalicylate, in which the quantity of Fe^{3+} and Sal^{2-} corresponded to the molar ratio of 1:1, was taken as the first component of the series; a solution of ammonium oxalate of the same concentration was taken as the second component. All solutions contained a fixed concentration of nitric acid. The pH values were measured by a quinhydrone electrode. The components of the series were mixed in different ratios with a constant total volume of 10 ml.

To reduce the error in the optical density measurements, we used somewhat different concentrations of isomolar series at different pH values of solution. Thus, the concentration of ferric nitrate (and of the oxalate respectively) in the series of experiments at pH 0.5 was $4 \cdot 10^{-3}$ mole/liter, at pH 1.3, 1.62 and 1.9 it was $2 \cdot 10^{-3}$ mole/liter and at pH 2.5 it was $1 \cdot 10^{-3}$ mole/liter.

TABLE 3

Exp. No.	$(NH_4)_2C_2O_4$ (mole/liter · $\cdot 10^4$)	D	$\bar{D}$	$-\lg[(NH_4)_2C_2O_4]$	$-\log \bar{D}$
1	0	0.91	–	–	–
2	0.4	0.83	0.08	4.40	1.10
3	0.6	0.79	0.12	4.22	0.92
4	0.8	0.75	0.16	4.10	0.79
5	1.0	0.72	0.19	4.00	0.72
6	1.2	0.68	0.23	3.92	0.63
7	1.4	0.64	0.27	3.85	0.57
8	1.6	0.59	0.32	3.80	0.49
9	1.8	0.56	0.35	3.74	0.45
10	2.0	0.53	0.38	3.70	0.42
11	2.4	0.45	0.46	3.62	0.34

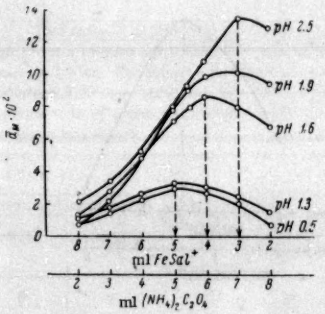

Fig. 3. Isomolar series of system $FeSal^+ - (NH_4)_2C_2O_4$ at different pH values of solution. Explanation in text.

Figure 3 shows a diagram of the properties of the studied system as a function of the pH of solution. For convenience of comparison, instead of the values for the change in optical density, the values for the decrease in optical density, referred to a 1 M solution, i.e., expressed in the units of the molar extinction coefficient, are used as ordinates. The values of $\bar{a}_M$ were obtained as usual by division of $\bar{D}$ by the value of the ferric nitrate concentration (in mole/liter) and by the height of the cell (in cm).

The figure shows that at pH ≈ 0.5-1.3 the simplest complex forms with a 1:1 component ratio. On increase of pH, the number of coordinated ions increases and the maximum shifts to the right. At pH > > 1.9 the number of coordinated oxalate ions is equal to 2, i.e., a complex $Fe(C_2O_4)_2^-$ evidently forms in the system. Evidently, on further increase of pH, formation of the complex anion $Fe(C_2O_4)_3^{3-}$ takes place which has the maximum number of coordinated groups.

Determination of the composition on other sections of the system. The investigated system may be represented in the form of a triangle $FeSCN^{2+} - C_2O_4^{2-} - H_2O$. The section parallel to the side $C_2O_4^{2-} - H_2O$ may be used to determine the composition of the complex. This section corresponds to the series of experiments with a constant concentration of ferric thiocyanate and a variable concentration of oxalate ion. The general form of the process may be expressed by equation:

$$FeSCN^{2+} + nC_2O_4^{2-} = Fe(C_2O_4)_n^{(3-2n)} + SCN^-. \qquad (6)$$

The equilibrium constant is equal to:

$$k_{equil\ (6)} = \frac{[Fe(C_2O_4)_n^{(3-2n)}][SCN^-]}{[C_2O_4^{2-}]^n[FeSCN^{2+}]} \qquad (7)$$

If a sufficient excess of potassium thiocyanate is added, then the concentration of [SCN⁻] will not change substantially when the equilibrium shifts. For simplicity, the same experiments may be used in which the decrease in optical density was not great in comparison to the initial optical density, i.e, then the concentration of [$FeSCN^{2+}$] may be considered approximately constant; in this case, Equation (7) is simplified:

$$\frac{[Fe(C_2O_4)_n^{(3-2n)}]}{[C_2O_4^{2-}]^n} = A \text{ (constant)} \qquad (8)$$

The logarithmic form of this equation is:

$$\log[Fe(C_2O_4)_n^{(3-2n)}] - n\log[C_2O_4^{2-}] + B = 0. \qquad (9)$$

Variation in concentration of $[Fe(C_2O_4)_n^{3-2n}]$ is proportional to the decrease in optical density $\bar{D}$. In sufficiently acidic solutions (pH<pK for $H_2C_2O_4$) only a small portion of the added oxalate is bound in complex; the free oxalate ion concentration may thus be considered directly proportional to the total concentration of added oxalic acid. Thus, on the basis of Equation (9) we may write:

$$\log \bar{D} - n\log[C_2O_{4\,total}^{2-}] + B = 0. \qquad (10)$$

If the values of the negative logarithm of the decrease in optical density and the negative logarithm of ammonium oxalate concentration are plotted in the same scale on a curve, then the slope of the curve will correspond to the value of n:

$$\tan \alpha = n. \qquad (11)$$

Table 3 gives the results of optical density measurements of a series of solutions containing ferric nitrate ($4 \cdot 10^{-4}$ mole/liter), a 10-fold excess of potassium thiocyanate ([KSCN] = $4 \cdot 10^{-3}$ mole/liter) and various amounts of ammonium oxalate from $0.4 \cdot 10^{-4}$ to $2.4 \cdot 10^{-4}$ mole/liter. All solutions were prepared in a medium containing 0.05 N nitric acid and were diluted to a fixed volume (10 ml) with this acid. The measurements were carried out at 465 mμ and for 10 mm layer thickness.

The given data show that as the concentration of ammonium oxalate increases 2,4 . . . times, the decrease of the color intensity changes also approximately by a factor of 2,4 . . . . Thus, the decrease in color intensity is linearly proportional to the oxalate concentration, i.e., the number of oxalate ions coordinated with iron is n = 1.

Figure 4 shows lines corresponding to n = 1,2 and 3 and the experimental data are represented as points. It is evident that the experimental points correspond to a line, the tangent of which is tan α = n = 1.

With this method we studied the equilibrium with the iron-salicylate complex. The results corresponded to tan α = n = 1.

Thus, the given data confirm the fact that the composition of the complex studied, under the given conditions, may be expressed by the formula $FeC_2O_4^+$.

Determination of the composition of complexes on the basis of light absorption study of isomolar series in the ultra-violet region of the spectrum. According to the available literature data, perchlorate ions do not absorb in the accessible ultra-violet region [9] and do not display any marked tendency towards complex formation [10]; therefore, a solution of ferric perchlorate was taken for the investigation of system $Fe^{3+} - H_2C_2O_4$ in ultra-violet light. The absorption spectra of aqueous solution of ferric perchlorate are described in the literature [11-13]. The intense band with a maximum near 240 mμ is ascribed to hydrated ferric ions. We measured the absorption spectrum of a $2 \cdot 10^{-4}$ M solution of ferric perchlorate in 0.1 N perchloric acid. The measurement was carried out on a SF-4 spectrophotometer for a layer thickness of 10 mm. The light absorption maximum was observed for a wave length near 240 mμ (Figure 5, Curve 2).

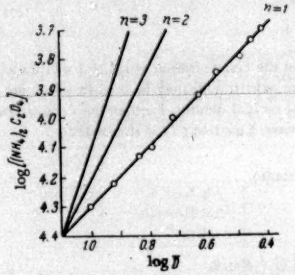

Fig. 4. Dependence of decrease of optical density on ammonium oxalate concentration. Explanation in text.

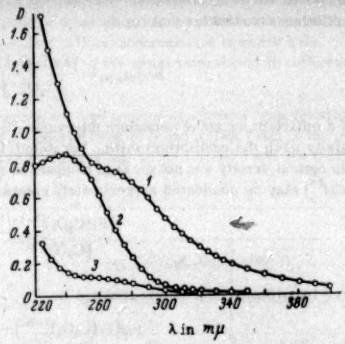

Fig. 5. Absorption spectra of solutions of iron-oxalate complex (1), ferric perchlorate (2) and sodium oxalate (3).

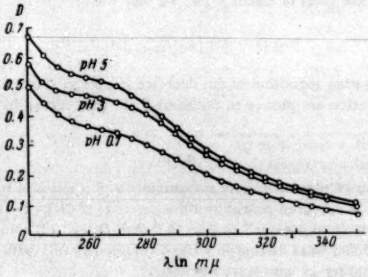

Fig. 6. Absorption spectra of solutions of iron-oxalate complexes at various pH values of solution.

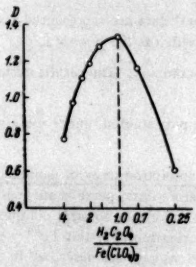

Fig. 7. Isomolar series of system $Fe(ClO_4)_3 - H_2C_2O_4$.

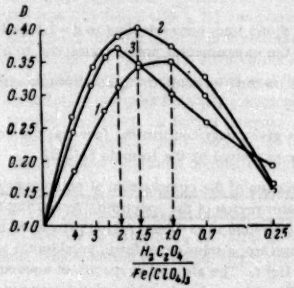

Fig. 8. Isomolar series of system $Fe(ClO_4)_3 - H_2C_2O_4$ at various concentrations of perchloric acid. 1) 0.1 M $HClO_4$, 2) 0.01 M $HClO_4$, 3) 0.002 M $HClO_4$.

On introduction of an excess of sodium oxalate in the system, the light absorption of the solution increases and the character of the curve changes (Figure 5, Curve 1). The concentration of ferric perchlorate was $2 \cdot 10^{-4}$ mole/liter, that of sodium oxalate $1 \cdot 10^{-3}$ mole/liter and that of $HClO_4$ 0.1 N. Curve 3 shows the absorption spectrum of sodium oxalate under the same conditions. A comparison of the curves of Figure 5 shows that the maximum difference in the light absorption between solutions of iron oxalate complex on the one hand and of ferric perchlorate on the other, is observed at 280-300 mμ.

Figure 6 shows the absorption spectra of the iron oxalate complex at different values of solution. It is evident that as the pH of solution increases, the light absorption by the solutions increases due to formation of complexes of different composition; however, the character of the curves remains the same.

To determine the composition of the iron oxalate complex, a system which contained $2 \cdot 10^{-3}$ M solutions of $Fe(ClO_4)_3$ and $H_2C_2O_4$ was studied by the isomolar-series method. All solutions contained 0.1 mole $HClO_4$ in 1 liter. The optical density of the solutions was measured at wave length 302.2 mμ. The comparison solutions were located in the second cell-holder; here were placed two cells (4.997 mm thick each); into one was run a solution of ferric perchlorate and into the other was run oxalic acid. The quantity of both cited components corresponded each time to the given investigated solution of the isomolar series. Thus, on passage of the light beam through these two consecutively placed cells, that portion of light was absorbed which corresponded to the given quantity of Fe^{3+} and $C_2O_4^{2-}$ ions which had not reacted. In the first cell these quantities were intermixed with each other. Consequently, the reading of the spectrophotometer directly characterizes the change of the optical density due to chemical reaction of Fe^{3+} and $C_2O_4^{2-}$. Figure 7 gives the results; the light absorption maximum is found at the ratio 1:1 of reacting components Fe^{3+} and $C_2O_4^{2-}$.

It was interesting to examine the change of the composition of the complex as a function of pH. The results of the optical density measurements are given in Figure 8.

Concentration of initial solutions: $[Fe(ClO_4)_3] = [H_2C_2O_4] = 5 \cdot 10^{-4}$ mole/liter. The concentration of perchloric acid was $2 \cdot 10^{-3}$ mole/liter (Curve 3), $1 \cdot 10^{-2}$ mole/liter (Curve 2) and $1 \cdot 10^{-1}$ mole/liter (Curve 1). The other conditions were the same as described previously. Measurements were taken at wave length 280.4 mμ.

SUMMARY

For the study of the iron oxalate complex, a method was used which involved physicochemical analysis of the solutions. The property of the system that was measured was the optical density. The determination of the composition of the iron complex which formed was carried out by investigation of the equilibrium with colored iron complexes and also the absorption spectra and the optical density of isomolar series in the ultraviolet portion of the spectrum.

It was shown that the composition of the complex at pH≤1 corresponded to a 1:1 ratio of Fe^{3+} and $C_2O_4^{2-}$. Aside from the above-mentioned $FeC_2O_4^+$, the complex anion $Fe(C_2O_4)^-$ also formed when the oxalate ion concentration increased, which was due, in particular, to the increase of the pH of solution to ≈ 2. At pH ≈ 2.5, $Fe(C_2O_4)_2^-$ predominated in the solution.

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VISCOSITY CALCULATIONS OF BINARY SYSTEMS. II

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Systems benzene-ethylbenzene, benzene-dibromoethane and benzene-methyl acetate were studied by the viscosity and density method.

After purification, the initial substances had b.p.: benzene 78.3° (727 mm), ethylbenzene 135.0° (737 mm), dibromoethane 130.4° (747 mm) and methyl acetate 55.9° (730 mm).

System benzene-ethylbenzene was studied at 25, 45 and 65°. The results of the viscosity and density measurements are given in Table 1. The viscosity curve at 25° shows a slight minimum, with increase of temperature the isotherm becomes a convex curve and at 65° becomes a straight line. The density values were converted to molar volumes. The diagram of molar volumes is characterized by straight lines.

System benzene-dibromoethane was studied at 25, 45 and 65°. The results of the measurements of viscosity and density are given in Table 2. The viscosity isotherms of this system are convex towards the axis of composition. The molar-volume isotherms of this system are curves which are concave towards the axis of composition.

System benzene-methyl acetate was studied at 25, 35 and 45°. The results of the viscosity and density measurements are given in Table 3. The viscosity isotherms are convex towards the axis of composition. The molar-volume isotherms are concave towards the axis of composition.

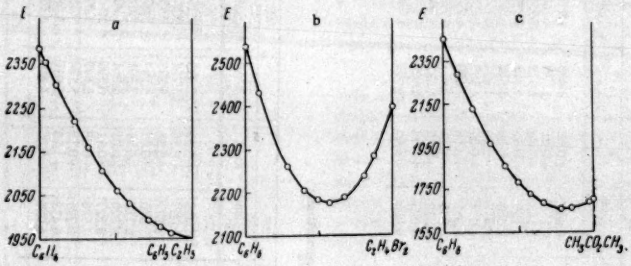

Diagram of "bond energy-composition" of the systems: benzene-ethylbenzene (a); benzene-dibromoethane (b), and benzene-methyl acetate (c).

Viscosity was calculated according to the slightly altered formula of Panchenkov [1]. The calculated viscosity values agreed well with the experimental data. Tables 1-3 give the calculated values of the viscosity of the investigated systems, which are given at two temperatures, since the experimental data on the viscosity at the third temperature were used for calculating the logarithm of constant A_η, which depends on the composition of the mixture. Tables 1-3 give also the values for the percentage deviation of the calculated viscosity value from the experimental value ($\Delta\eta\%$) the bond energy of the mixture molecules (E_c), the bond energy of

TABLE 1

System Benzene-Ethylbenzene

C_6H_6 (mole %)	25°			45°			65°	$E_{1,2} = 1952.8$		Density		
	$\eta_{exp.} \cdot 10^3$	$\eta_{calc.} \cdot 10^3$	$\Delta\eta$ %	$\eta_{exp.} \cdot 10^3$	$\eta_{calc.} \cdot 10^3$	$\Delta\eta$ %	$\eta_{exp.} \cdot 10^3$	E_η	Log A_η	25°	45°	65°
0.00	6.283	6.285	+0.03	5.038	5.040	+0.04	4.128	1953.9	$\bar{5}.24863$	0.8617	0.8438	0.8261
14.50	6.185	6.198	+0 21	4.939	4.964	+0.51	4.042	1962.9	$\bar{5}.23527$	0.8621	0.8441	0.8255
21.47	6.165	6.145	−0.32	4.912	4.918	+0 12	4.014	1976.6	$\bar{5}.22008$	0.8630	0.8449	0.8261
29.42	6.156	6.126	−0.49	4.912	4.880	−0.65	3.988	1991.9	$\bar{5}.20632$	0.8636	0.8443	0.8260
41.87	6.078	6.066	−0.20	4.812	4.823	+0.23	3.920	2030.9	$\bar{5}.17093$	0.8649	0.8456	0.8265
49.44	6.057	6.057	0.00	4.774	4.798	+0.50	3.892	2061.4	$\bar{5}.14577$	0.8655	0.8456	0.8266
59.26	6.038	6.034	−0.05	4.737	4.759	+0.46	3.842	2108.7	$\bar{5}.10698$	0.8660	0.8458	0.8262
68.87	6.029	6.059	+0.50	4.690	4.759	+1.47	3.821	2163.2	$\bar{5}.06578$	0.8672	0.8475	0.8270
77.86	6.012	6.035	+0.38	4.657	4.705	+1.03	3.761	2223.7	$\bar{5}.01644$	0.8688	0.8478	0.8274
89.38	6.006	6.030	+0.40	4.621	4.666	+0.97	3.697	2306.9	$\bar{6}.95067$	0.8714	0.8494	0.8284
95.68	6.008	6.023	+0.24	4.607	4.634	+0.59	3.661	2358 6	$\bar{6}.91032$	0.8721	0.8504	0.8293
100.00	6.029	6.026	−0.05	4.600	4.625	+0.54	3.645	2396.2	$\bar{6}.88133$	0.8727	0.8515	0 8305

TABLE 2

System Benzene- Dibromoethane

C_6H_6 (mole %)	25°			45°			65°	$E_{1,2} = 1889.8$		Density		
	$\eta_{exp.} \cdot 10^3$	$\eta_{calc.} \cdot 10^3$	$\Delta\eta$ %	$\eta_{exp.} \cdot 10^3$	$\eta_{calc.} \cdot 10^3$	$\Delta\eta$ %	$\eta_{exp.} \cdot 10^3$	E_η	Log A_η	25°	45°	65°
0.00	16.031	16.035	+0.02	12.073	12.156	+0.69	9.589	2540.1	$\bar{6}.66945$	2.1665	2.1229	2.0845
8.88	14.146	14.067	−0.56	10.764	10.848	+0.78	8.504	2433.7	$\bar{6}.72841$	2.0445	2.0075	1.9561
21,10	12.244	12.179	−0.53	9.373	9.451	+0.83	7.536	2317.2	$\bar{6}.80098$	1.8860	1.8459	1 8080
29.04	11.079	11.030	−0.45	8.544	8.629	+0.99	6.912	2259.9	$\bar{6}.83620$	1.7775	1.7428	1.7073
40.62	9.740	9.712	−0.29	7.591	7.622	+0.41	6.128	2202.6	$\bar{6}.87555$	1 6283	1.5947	1.5610
49.51	8.819	8.820	+0.01	6.861	6.920	+0.86	5.574	2179.7	$\bar{6}.89409$	1.5122	1.4785	1.4474
56.87	8.218	8.227	+0.11	6.399	6.466	+1.05	5.203	2174.5	$\bar{6}.90549$	1.4173	1.3867	1.3563
66.85	7.534	7.528	−0.08	5.849	5.890	+0.87	4.725	2187.5	$\bar{6}.90752$	1.2987	1.2675	1.2377
80.82	6.718	6.726	+0.12	5.184	5.252	+1.32	4.194	2244.5	$\bar{6}.90401$	1.1133	1.0890	1.0634
86.77	6.493	6.413	−1.23	5.010	4.980	−0.60	3.992	2282.9	$\bar{6}.89342$	1.0399	1.0157	0.9969
100.00	6.029	6.026	−0.05	4.600	4.625	+0.54	3.645	2396.2	$\bar{6}.88133$	0.8727	0.8515	0.8305

TABLE 3

System Benzene-Methyl Acetate

C_6H_6 (mole %)	25°			35°			45°	$E_{1,2}$ = 1478.2		Density		
	$\eta_{exp.} \cdot 10^4$	$\eta_{calc.} \cdot 10^4$	$\Delta\eta$ %	$\eta_{exp.} \cdot 10^4$	$\eta_{calc.} \cdot 10^4$	$\Delta\eta$ %	$\eta_{exp.} \cdot 10^4$	E_0	Log A_2	25°	35°	45°
0.00	3.659	3.675	+0.45	3.293	3.305	+0.35	2.962	1701.7	5.17668	0.9259	0.9137	0.8989
13.77	3.802	3.785	—0.45	3.427	3.397	—0.87	3.073	1662.8	5.22766	0.9160	0.9028	0.8893
23.11	3.965	3.940	—0.63	3.554	3.511	—1.21	3.210	1652.0	5.24967	0.9100	0.8974	0.8855
33.90	4.098	4.115	+0.41	3.685	3.687	+0.05	3.319	1688.0	5.24924	0.9029	0.8916	0.8784
42.56	4.297	4.249	—1.07	3.829	3.803	—0.68	3.450	1728.7	5.23537	0.8978	0.8862	0.8750
50.41	4.424	4.423	—0.02	3.956	3.966	+0.25	3.563	1781.2	5.21244	0.8942	0.8825	0.8706
59.43	4.628	4.627	—0.02	4.135	4.134	—0.02	3.714	1859.8	5.17205	0.8894	0.8776	0.8661
68.93	4.884	4.883	—0.02	4.333	4.345	+0.28	3.888	1963.6	5.11598	0.8849	0.8737	0.8624
81.12	5.291	5.279	—0.23	4.663	4.669	+0.13	4.144	2128.5	5.02421	0.8802	0.8697	0.8577
91.09	5.661	5.650	—0.19	4.964	4.953	—0.22	4.377	2289.9	4.93247	0.8759	0.8647	0.8543
100.00	6.029	6.029	0.00	5.254	5.247	—0.13	4.600	2454.4	4.83584	0.8727	0.8619	0.8515

the molecules of the first component with the molecules of the second component ($E_{1,2}$). Calculation of the values of E_0, $E_{1,2}$ and log A_2 was carried out as described in Panchenkov's monograph [2].

Curves of the dependence of the bond energy of the molecules on composition (see diagram) were plotted. The "bond energy-composition" curve of system benzene-ethylbenzene is convex towards the axis of composition. Curves of systems benzene-dibromoethane and benzene-methyl acetate pass through the minimum.

Correlation of the data on viscosity, molar volumes, and bond energy, shows that there is no chemical affinity between the components of system benzene-ethylbenzene. The cryoscopic molecular-weight determinations that were carried out also indicate an absence of molecular change: in benzene the molecular weight of ethylbenzene remained constant. The dependence of the partial pressures of the components of this system on composition is expressed by a straight line [3].

The components of the system benzene-dibromoethane and benzene-methyl acetate also show no chemical interaction between each other; however, in the formation of these systems, some expansion occurs. An indication of expansion in systems benzene-dibromoethane and benzene-methyl acetate are the molar-volume isotherms and the bond energy-composition curves (see diagram) which are concave towards the axis of composition.

Kireev's data [4] give the expansion in system benzene-dibromoethane as 0.225 cm^3 and the heat effect of solution-formation as -68.7 cal.

Cryoscopic measurements in benzene of the molecular weight of dibromoethane and methyl acetate (Tables 4 and 5) showed slight deviations from the constant value of the molecular weight of dibromoethane and methyl acetate. The presence of the slight association of methyl acetate was confirmed by inspecting the vapor-pressure curve of system benzene-methyl acetate, which was concave towards the axis of composition [5].

The results of calculating the bond energy are given in Tables 2 and 3 and show that upon mixing benzene with dibromoethane and benzene with methyl acetate, the bond between the component molecules weakens. The value of the bond energy of the molecules of the first component with molecules of the second ($E_{1,2}$) is much less than that of the bond energy of the pure components. The dependence of the bond energy of the molecules on composition is expressed by a curve with a minimum.

TABLE 4

Molecular Weight of Dibromoethane in Benzene

Taken benzene (in g)	Taken dibromoethane (in g)	Δ T	Moles dibromoethane in 1000 g benzene	Molecular weight
12.13	0.4021	0.907	0.177	184.5
11.08	0.4609	1.137	0.221	184.0
12.13	0.6928	1.537	0.304	185.8
11.08	1.1263	2.718	0.541	183.6
11.08	1.8552	4.327	0.891	185.0
11.08	1.9459	4.464	0 935	187.7
11.08	2.8298	6.312	1.359	187.2
11.08	3.7071	8.033	1.781	187.1
11.08	4.2665	9.031	2.010	188.3
11.08	4.9424	10.216	2.374	188.7

TABLE 5

Molecular Weight of Methyl Acetate in Benzene (Benzene taken 11.31 g)

Taken methyl acetate (in g)	Δ T	Moles methyl acetate in 1000 g benzene	Molecular weight
0.1274	0.760	0.152	75.0
0.2477	1.450	0.296	75.6
0.3943	2.269	0.471	75.9
0.5635	3.186	0.673	76.2
0.7654	4.205	0.914	77.1
0.8260	4.499	0.983	77.4
1.1507	6.058	1.374	78.0
1.3063	6.752	1.560	78.6
1.4618	7.467	1.745	78.5
1.6296	8.180	1.946	79.0

"Bond energy-composition" curves that pass through a minimum were also obtained by calculation of systems benzene-dichloroethane and benzene-iodobenzene according to literature data. System benzene-dichloroethane was studied by Kireev and Skvortsova [6] and Faust [7]. The divergence between the data of these authors on viscosity and density values results in disagreement between the bond energy curves but in both cases the dependence of bond energy on composition is expressed by a curve with a sharp minimum. System benzene-dichloroethane forms with an expansion. According to Kireev's data [4], the expansion is 0.243 cm^3, and the heat effect is -17.4 cal.

For calculation of the bond energy of the molecules of system benzene-iodobenzene, viscosity and density data from the work of Meyer and Mylius [8] were used. On converting density to molar volumes, we obtained a molar-volume curve which was convex towards the axis of composition. Consequently, on mixing benzene with iodobenzene, expansion takes place.

Thus, in systems which form with expansion but without chemical interaction, the "bond energy-composition" diagram shows a minimum which indicates weakening of the bond between component molecules upon mixing.

SUMMARY

1. Systems benzene-ethylbenzene, benzene-dibromoethane and benzene-methyl acetate were studied by the viscosity-density method.

2. The molecular weights of ethylbenzene, dibromoethane and methyl acetate in benzene were determined (cryoscopically).

3. Calculation of viscosity for the studied systems was according to Panchenkov's formula and the calculated values for the viscosity agreed well with the experimental data.

4. The presence of a minimum on the "bond energy-composition" curve characterizes the system as having an expansion without chemical interaction of components.

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A NEW SYNTHESIS OF IMIDODISULFONATES

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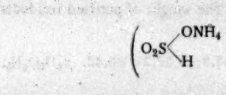
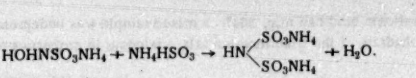
Several methods are known for the preparation of imidodisulfonates: the reaction of ammonia with either sulfur trioxide or with chlorosulfonic acid, the hydrolysis of the nitrilotrisulfonate [1], and the pyrolysis of ammonium sulfamate [2]. To us it seemed more convenient to obtain the imidodisulfonates from the readily available hydroxylamine monosulfonate and the salts of sulfurous acid. In order for these substances to react with each other and form the imide, it is necessary that the salt of the sulfurous acid have an unsymmetrical structure. According to much data [3,4], the bisulfites possess such a structure.



In addition, in studying analogous reactions, Raschig [3] established that hydroxylamine sulfate even in the cold reacts with the bisulfite to give sulfamic acid. The nitrilotrisulfonate was obtained when the bisulfite was heated with hydroxylamine disulfonate (I); consequently, to synthesize diammonium imidodisulfonate (II) we used a neutral solution of ammonium hydroxylamine-O-sulfonate (III) and ammonium bisulfite:



(III) (II)

The hydroxylamine monosulfonate used in this reaction was prepared under some modification of the Raschig method [3] via the hydroxylamine disulfonate (I) from sodium nitrite, ammonium bisulfite and sulfur dioxide. The imidodisulfonate (II) was prepared at a temperature of 45-50°, where the reaction proceeded quite rapidly. The yield of the imidodisulfonate was 50-65% (when calculated on the basis of III). To prove its structure the obtained substance was subjected to hydrolysis in the presence of H_2SO_4, both in the cold and under heating. Ammonium sulfamate and ammonium sulfate were respectively obtained. The treatment of (II) with excess ammonia [5] gave the monohydrate of triammonium imidodisulfonate.

In the present study we also showed considerable simplification of the elaborate method [5] for the preparation of sulfamic acid from hydroxylamine and sulfur dioxide. Reaction between the components of this reaction proceeds slowly, and in addition, the use of pressure is necessary to obtain a satisfactory yield of the sulfamic acid. This apparently is explained by the structure of sulfurous acid [3], unfavorable for the given reaction. In order to have the reaction run rapidly and at atmospheric pressure, we replaced the sulfur dioxide by ammonium bisulfite. As was indicated, the reaction between hydroxylamine and the bisulfite had already been studied by Raschig, but he failed to utilize this reaction as a method for the preparation of sulfamic acid, and only limited himself to its analytical determination in solution. We added concentrated H_2SO_4 to the reaction product from hydroxylamine sulfate and ammonium bisulfite, which liberated the sulfamic acid from its aqueous ammonium salt solution and at the same time lowered the sulfamic acid solubility [6] in water. As the result of numerous experiments we established the optimum amount of added sulfuric acid, assuring the precipitation of pure sulfamic acid

from the solution, and not of its mixture with either the bisulfite or the binary salt $(NH_4)_2SO_4 \cdot HOSO_2NH_2$ [7]; here we obtained sulfamic acid in 65-70% yield, based on hydroxylamine sulfate.

EXPERIMENTAL

Diammonium salt of imidodisulfonic acid (II). To an aqueous solution of $NaNO_2$ (concentration 145 g/liter) an equimolecular quantity of an aqueous solution of NH_4HSO_3 (concentration 830 g/liter) was added with stirring and then SO_2 was passed until a slightly acid reaction was obtained on methyl orange. The temperature was held in the range $0 \pm 2°$. The resulting solution of the sodium-ammonium salt of hydroxylaminodisulfonic acid (I) was set aside at room temperature for 24 hours. Due to hydrolysis of (I) the resulting solution contained 225 g/liter hydroxylamine monosulfonate (calculated on the ammonium salt). To establish the concentration of (III) it was hydrolyzed, by boiling with H_2SO_4, to hydroxylamine, which was determined according to Raschig [8]. 1.5 liter solution of hydroxylamine monosulfonate (III) with an acidity of 83.3 g/liter (calculated on H_2SO_4) was neutralized by ammonia at a temperature which did not exceed +3°. After neutralization, the solution was steamed down (during this the medium was kept slightly alkaline by addition of ammonia) and the precipitate which came down was filtered off. This operation was repeated three times. The precipitates weighed 203, 134 and 31 g; sodium sulfate predominated in the first of them and in the last - ammonium sulfate. Yield 353 g of viscous syrup (d_4^{20} 1.62), which contained 62% ammonium hydroxylamine-O-sulfonate (III).

27.5 g of (III) was run with stirring into 15 ml of 61% aqueous NH_4HSO_3 solution; the temperature was maintained in the range 45-50° by cooling. After 30 minutes, the temperature fell to room temperature, at which temperature stirring was continued for 2 hours. The white precipitate which came down was filtered off and washed with 12 ml 90% aqueous methanol and 20 ml ether. The weight of purified imidodisulfonate (II) was 14.4 g (52%, calculated on III).

Found %: N (total) 19.9; N (ammonium [9]) 13.3; S 30.21, 30.42. $S_2H_9O_6N_3$. Calculated %: N (total) 19.89; N (ammonium) 13.26; S 30.32.

10 g of the diammonium salt of imidodisulfonic acid (II) was dissolved in 20 ml water and at a temperature not above 50° 18 ml concentrated H_2SO_4 was added. After 24 hours of standing at room temperature, the precipitate that came down was separated and washed with methanol.

Found %: N (total) 14.3; N (ammonium) 0.2. SH_3O_3N. Calculated %: N (total) 14.42; N (ammonium) 0.

The obtained amidosulfonic acid had m.p. 204°; a mixed sample was undepressed. Treatment of (II) with ammonia yielded the monohydrate of the triammonium salt, analogous in properties to the compound described in the literature [5].

Sulfamic acid. Into a flask fitted with stirrer was run 30 ml commercial NH_4HSO_3 solution with a concentration of 830.7 g/liter. To this on stirring, was added 10 g hydroxylamine sulfate in small portions in the course of 40 minutes; during this the temperature was held at 15-25°. After 30 minutes had elapsed, 15.5 ml concentrated H_2SO_4 (d_4^{20} 1.831) was run into the contents of the flask upon cooling. The white precipitate which came down was filtered off. Yield 7.7 g sulfamic acid (65% on hydroxylamine). The impure product contained 0.78% ammonium nitrogen. After recrystallization from water [5], sulfamic acid contained no ammonium nitrogen and had m.p. 206°.

SUMMARY

1. A method was developed for the preparation of the imidodisulfonate from the hydroxylamine monosulfonate.

2. The method for the preparation of sulfamic acid from hydroxylamine sulfate was improved.

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SOME ESTERS OF BUTANEARSONOUS ACID

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The esters of alkanearsonous acids are slightly studied compounds. All of the information on them is limited to the work of Ya. F. Komissarov and coworkers [1], where the boiling points and densities of five esters of methanearsonous and ethanearsonous acids are given. In the meantime a study of the properties of the esters of alkanearsonous and dialkanearsonous acids can reveal rules in property changes when going from the neutral esters of arsenious acid to the tertiary arsines.

The purpose of the present study was to synthesize and study the properties of some esters of n-butanearsonous acid. The esters were synthesized by heating n-butylarsine oxide with the proper alcohol in the presence of anhydrous copper sulfate by the reaction:

$$C_4H_9AsO + 2ROH \rightarrow C_4H_9As(OR)_2 + H_2O.$$

As the result of this work we synthesized five esters of n-butanearsonous acid, measured their molecular refraction for the D line and calculated the atomic refraction of arsenic, on the average equal to 10.42. The physicochemical constants of the esters are given in Table 1. The esters are readily hydrolyzed by moist air,

TABLE 1

Ester of the butanearsonous acid	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D	Atomic refraction of As
Methyl	65—67° (15)	1.1869	1.4555	44.39	10.1
Ethyl	81—83 (15)	1.1072	1.4495	53.86	10.33
n-Propyl	104—106 (12.5)	1.0617	1.4515	63.51	10.74
n-Butyl	132—134 (14)	1.0389	1.4540	72.46	10.46
n-Octyl	193—195 (6)	0.9777	1.4603	109.43	10.48

and show rapid oxidation with the formation of crystalline compounds. An attempt to prepare the esters of n-butanethioarsonous acid by the addition of sulfur to the esters of n-butanearsonous acid ended in failure: sulfur was not added when the esters of n-butanearsonous acid were reacted directly.

To study the arrangement of the hydrocarbon chains in the esters of n-butanearsonous acid we determined the parachors of the n-propyl and n-butyl esters. A comparison of the experimentally found parachors with those theoretically calculated by the Gibling method [2] for the two possible structure variations revealed that the long ester chains in the esters of n-butanearsonous acid are arranged parallel to each other. However, a conclusive answer to the problem of the structure of the esters of n-butanearsonous acid requires much additional data.

EXPERIMENTAL

The initial butylarsine oxide was a viscous liquid with b. p. 177-178° at 1.5 mm and d_4^{20} 1.1170.

For synthesis of n-butanearsonous acid esters, in a 3-necked flask fitted with reflux condenser, through a short adapter with an inserted cartridge of filter paper and anhydrous copper sulfate, was placed the butylarsine oxide and into this was run a large excess (3-5 fold quantity) of the corresponding alcohol. In the case of the methyl and ethyl esters, the copper sulfate was placed directly in the reaction flask. The mixture was then heated to the boil for 2 hours and then the alcohol excess was driven off and the residue was vacuum-distilled. All the synthesis and distillation operations were carried out in a CO_2 atmosphere.

The surface tension was determined by the method of the greatest bubble pressure. Surface tension values, yields and analytical data on the synthesized n-butylarsinic acid esters are given in Table 2.

TABLE 2

Compound	Yield (in %)	Content As (in %) Found	Content As (in %) Calculated	γ^{20} (dyne/cm)	Parachor
n-$C_4H_9As(OCH_3)_2$	40.3	38.46	38.60	—	—
n-$C_4H_9As(OC_2H_5)_2$	37.1	33.56	33.72	—	—
n-$C_4H_9As(On\text{-}C_3H_7)_2$	64.4	29.65	29.94	26.1	532.6
n-$C_4H_9As(On\text{-}C_4H_9)_2$	76.6	26.86	26.92	—	—
n-$C_4H_9As(On\text{-}C_8H_{17})_2$	86.2	19.10	19.19	28.8	925.1

SUMMARY

Five esters of n-butanearsonous acid (methyl, ethyl, n-propyl, n-butyl and n-octyl) have been described for the first time.

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SYNTHESIS OF SOME MERCAPTANS AND DISULFIDES LABELED WITH RADIOACTIVE SULFUR ISOTOPE

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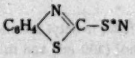
The methods used to introduce the radioactive sulfur isotope S^{35} into the molecules of organic compounds can vary and are essentially determined by the composition and structure of the substances being synthesized. In a number of cases the radioactive sulfur isotope can be introduced into the molecule by the method of isotopic exchange between the corresponding substance and elementary radioactive sulfur. This method was used to obtain labeled thiourea $(NH_2)_2CS^*$ [1], sodium diethyldithiocarbamate $(C_2H_5)_2N-CS^*-SNa$ [1], 2-mercaptobenzothiazole, labeled in the mercapto group [1, 2],



tetramethylthiuram disulfide, labeled in all four sulfur atoms $(CH_3)_2N-C^*S-S^*-S^*-CS^*-N(CH_3)_2$ [3], and others. However, many sulfur compounds fail to enter into exchange reaction with elementary sulfur, or together with the exchange reaction, there proceed various side reactions, making substance purification difficult, etc.; consequently, the labeled atom is introduced into various compounds by chemical synthesis.

Comparatively much work has been published in the literature on the synthesis of S^{35} labeled compounds. * Having studied the influence of molecular structure on the mobility of sulfur atoms by the method of labeled atoms, we synthesized a number of mercaptans and disulfides containing the radioactive sulfur isotope.

Some of the labeled mercaptans, monosulfides and disulfides could be synthesized by making use of the mobility of the halogen atom in the proper organic compound and running the reaction between this substance and the proper alkali metal sulfur compound labeled with isotopic sulfur, i.e., the S^{35}-labeled compound could be obtained by one of the following reactions:

$$RX + Me\overset{*}{S}H \rightarrow R\overset{*}{S}H + MeX,$$

$$2RX + Me_2\overset{*}{S} \rightarrow R\overset{*}{S}R + 2MeX,$$

$$2RX + Me_2\overset{*}{S}_2 \rightarrow R\overset{*}{S} - \overset{*}{S}R + 2MeX.$$

* See, for example, the survey by S. L. Thomas, H. S. Turner in Quart. Rev., 407 (1953).

where RX designates the halogen compound, and Me the monovalent metal (sodium, potassium, ammonium).

We made use of the ability for replacement of a halogen atom by either the sulfhydryl, sulfide or disulfide group to synthesize S^{35}-labeled compounds containing alkyl, p-nitrophenyl and benzothiazolyl [4] radicals.

For most aromatic compounds the halogen atom linked to the aromatic nucleus is inert, and consequently the above reactions cannot be used to synthesize S^{35}-labeled aromatic compounds. Introduction of isotopic sulfur into aromatic mercaptans and disulfides can be realized through the organomagnesium compounds, and also through diazo compounds. We made use of these methods to obtain labeled compounds containing the phenyl, tolyl, methoxyphenyl and biphenyl radicals.

In the present study we failed to pursue the goal of obtaining preparations with a high specific activity, for which reason we ran the syntheses not on a micro scale, as is frequently done for the synthesis of radioactive compounds, but instead we prepared the radioactive substances in comparatively large amounts (of the order of tens of grams) with a total activity of 1-5 mCu. In principle the method for obtaining preparations with a greater specific activity may not differ from the method used by us; if more active compounds are desired it is necessary to operate with smaller amounts of substances and to take starting sulfur compounds with a greater specific activity. For our study of the isotopic exchange reaction we needed preparations showing comparatively low specific activity (μCu), for which reason we at times diluted the radioactive preparations obtained in our synthesis with the corresponding unlabeled substance.

To determine the activity of the sulfur in our synthesized preparations the latter were oxidized by the Carius method, and the $S^*O_4^{2-}$ was precipitated with benzidine hydrochloride. The syntheses of a number of labeled mercaptans and disulfides are described below. A summary of the syntheses is given in the table.

EXPERIMENTAL

n-Butylmercaptan-S^{35} was synthesized from n-butyl bromide and radioactive sodium hydrosulfide. Metallic sodium (5 g) was dissolved in ethyl alcohol (100 ml) and the solution was saturated with hydrogen sulfide until formation of sodium hydrosulfide. Radioactive sulfur was introduced into solution either in the form of hydrogen sulfide or in the form of elementary sulfur. In the first case, a portion (~ 10 ml) of the solution of metallic sodium in alcohol was saturated with radioactive hydrogen sulfide and this portion was then added to the main NaSH solution. In the second case, to the alcoholic sodium solution was added a small amount (0.01-0.005 g) of elementary sulfur S^{35} with a total activity of 1-2 m Cu and ordinary hydrogen sulfide was passed through the solution. As sodium sulfide formed, the radioactive sulfur dissolved. When solution went slowly, the solution was heated on a water bath and after solution of the sulfur, into the cooled solution was passed hydrogen sulfide until NaSH formed. Thus, a solution of radioactive sodium hydrosulfide in alcohol was obtained.

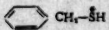
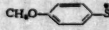
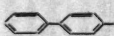
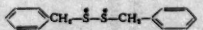
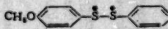
All operations in the preparation of radioactive sodium hydrosulfide were carried out in an atmosphere of dry nitrogen. 30 g n-butyl bromide was carefully added to a solution of Na*SH in alcohol in a flask fitted with reflux condenser and dropping funnel; toward completion of the reaction, the whole mass was heated on a water bath for 2-3 hours. On cooling, the reaction mixture was poured in water, the precipitate of sodium bromide dissolved and the butylmercaptan separated out as an oil. The oil was extracted with ether, the ethereal layer was separated off, dried with fused calcium chloride and after driving off the ether, the product was distilled. The fraction was collected with b. p. 98°.

The yield was 80-90%. The activity of the butylmercaptan was determined by the activity of initial sulfur or of hydrogen sulfide, discounting the dilution with unlabeled hydrogen sulfide.

Benzylmercaptan-S^{35} was synthesized from benzyl chloride and radioactive sodium hydrosulfide by a method similar to the above. The oily benzylmercaptan which separated out was extracted from the reaction mixture with ether and after drying the solution with calcined sodium sulfate and driving off the ether, it was distilled.

This method of synthesis is probably applicable to the preparation of labeled mercaptans with any desired alkyl groups.

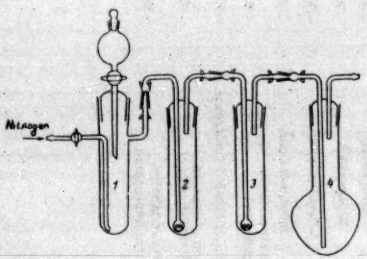
Syntheses of S^{35}-labeled compounds

S^{35}-labeled compound	Structural formula	Method of synthesis	Yield (in %)	Constant of product
n-Butylmercaptan	$C_4H_9\overset{*}{S}H$	$C_4H_9Br+Na\overset{*}{S}H$	~80	B.p. 98°
Benzylmercaptan		$C_6H_5CH_2Cl+Na\overset{*}{S}H$	~75	B.p. 195°
p-Thiocresol		p-Tolylmagnesium bromide and $\overset{*}{S}_8$	~20—25	M.p. 43°
p-Methoxythiophenol		Diazo-compound of p-anisidine and $C_2H_5O-C\overset{*}{S}-\overset{*}{S}K$	~70	B. p. 89° (4 mm)
Biphenylmercaptan		Diazo compound of biphenylamine and $C_2H_5-O-C\overset{*}{S}-\overset{*}{S}K$	~70	M.p. 109°
Potassium ethylxanthate	$C_2H_5O-C\overset{*}{S}-\overset{*}{S}K$	$Na_2\overset{*}{S}+CS_2 \rightarrow Na_2C\overset{*}{S}_3$ $Na_2C\overset{*}{S}_3 \rightarrow Na_2\overset{*}{S}+C\overset{*}{S}_2$ $C\overset{*}{S}_2+C_2H_5OK$	60—80	—
Diethyl disulfide	$C_2H_5-\overset{*}{S}-\overset{*}{S}-C_2H_5$	$2C_2H_5I+Na_2\overset{*}{S}_2$	~80	B.p. 47—48°(10 mm)
n-Dibutyl disulfide	$C_4H_9-\overset{*}{S}-\overset{*}{S}-C_4H_9$	$2C_4H_9Br+Na_2\overset{*}{S}_2$	~90	B.p. 229°
Dibenzyl disulfide		$C_6H_5-CH_2Cl+Na_2\overset{*}{S}_2$	~90	M.p. 77°
p,p-Dinitrodiphenyl disulfide		$2NO_2C_6H_4Cl+Na_2\overset{*}{S}_2$	~50	M.p. 179°
Diphenyl disulfide		Phenylmagnesium bromide and $\overset{*}{S}_2Cl_2$	~30	M.p. 60.5°
Di-p-tolyl disulfide		Oxidation of labeled thiocresol	~90	M.p. 46°
Di-p-methoxydiphenyl disulfide		Oxidation of labeled methoxythiophenol	~80	M.p. 44°
Di-p-biphenyl disulfide		Oxidation of labeled biphenylmercaptan	~80	M.p. 149.5°

p-Thiocresol-S^{35} was synthesized by the reaction between p-tolylmagnesium bromide and elementary radioactive sulfur.

The method of synthesis was similar to the method of synthesis of labeled thiocresol as described in literature [5].

A Grignard reagent was prepared from p-bromotoluene (53 g) and magnesium filings (7.5 g) in absolute ether. Finely pulverized radioactive elementary sulfur (10 g) with a total activity of 2-3 m Cu was suspended in the dry ether and into this suspension the Grignard reagent was slowly run through the dropping funnel with stirring. The reaction mass was then heated for 2 hours on a water bath. On cooling, the resulting complex was decomposed with cooled dilute hydrochloric acid (1:7) with strong cooling of the reaction mixture (ice with salt) and vigorous stirring. Upon decomposition of the complex, side by side with formation of thiocresol there separated out radioactive hydrogen sulfide which was removed by a stream of nitrogen and absorbed by alkali. The prepared thiocresol was extracted from the reaction mixture with ether. The ethereal extract was treated with 10% alkali solution and from this alkaline solution thiocresol was separated out with acid and again extracted with ether. After drying the ethereal fraction and driving off the ether, thiocresol was vacuum-distilled, b. p. 77° (10 mm), m. p. 43°. Yield of labeled thiocresol was 20-25%.



Apparatus for preparing radioactive sodium trithiocarbonate, carbon bisulfide and potassium ethylxanthate. Explanation in text.

Together with thiocresol in this synthesis there formed labeled ditolyl disulfide, which remained in ethereal solution after treatment of the latter with alkali. Labeled ditolyl disulfide, m. p. 46°, was obtained by recrystallization of the product which remained after the ether was steamed off.

p-Methoxythiophenol-S^{35}. On the basis of the synthesis of labeled methoxythiophenyl a general reaction was formulated for the synthesis of aromatic mercaptans through diazo compounds [6]. The synthesis was carried out in several stages and involved the preparation of a number of S^{35}-labeled compounds: sodium trithiocarbonate, carbon bisulfide and potassium ethylxanthate. Radioactive sodium trithiocarbonate, carbon bisulfide and potassium ethylxanthate were prepared in the apparatus depicted in the illustration. In the apparatus a nitrogen atmosphere was created and in Vessel 1 was introduced a solution of $Na_2S \cdot 9H_2O$ (7.5 g) in alcohol (10 ml) and a small quantity ($\sim$0.001 g) of radioactive crystalline sulfur with an activity of 1-2 m Cu. The apparatus was sealed and the solution was set aside overnight; the sulfur dissolved. Into the solution of radioactive sodium sulfide in Vessel 1 was then run carbon bisulfide (2.5 g), and sodium trithiocarbonate $Na_2C\,{}^*S_3$ was obtained. In special experiments (carried out in conjunction with L. Barn), we established that the sulfur atoms in sodium trithiocarbonate, prepared from radioactive sodium sulfide and carbon bisulfide, are equivalent. On decomposition of radioactive sodium trithiocarbonate (separated out as lustrous yellow crystals) with acid, hydrogen sulfide and carbon bisulfide formed:

$$Na_2C\overset{*}{S}_3 + 2HCl \rightarrow H_2\overset{*}{S} + C\overset{*}{S}_2 + 2NaCl,$$

in which hydrogen sulfide contained $^1/_3$ and carbon bisulfide $^2/_3$ of the radioactive isotope of the initial sodium sulfide.

In carrying out the given synthesis, sodium trithiocarbonate did not separate out but decomposed in hydrochloric acid solution. The hydrogen sulfide which separated out was removed from Vessel 1 by nitrogen and

absorbed in Traps 2 and 3 by a saturated solution of cadmium acetate. Radioactive carbon bisulfide, obtained on decomporing sodium trithiocarbonate, was collected by a solution of potassium ethylate in alcohol (Vessel 4). The potassium ethylate solution was prepared by solution of metallic potassium (1.25 g) in ethyl alcohol (100 ml). For completeness of evolution of carbon bisulfide, Vessels 1, 2 and 3 were placed in a water bath and heated to 60°. The radioactive potassium ethylxanthate which formed in Vessel 4 was diluted with the unlabeled product (5-10 g) precipitated from alcoholic solution with ether, filtered off, washed with ether, dried in a vacuum-desiccator and was then used further for the synthesis of labeled p-methoxythiophenol. All synthetic and separation operations for potassium ethylxanthogenate were carried out in an atmosphere of nitrogen. Labeled p-methoxythiophenol was prepared in the following manner. A solution of labeled potassium ethylxanthate (50 g) in water (120 ml) was placed in a round-bottomed flask fitted with stirrer, dropping funnel and outlet tube. The ratio of lebeled and unlabeled potassium ethylxanthate may be varied, depending on what activity the preparation requires for the further work. The solution was heated to 70-75° and into this was slowly run drop-wise a solution of diazo-p-anisidine hydrochloride, prepared from 20.5 g p-anisidine; abundant evolution of nitrogen took place. After this, the whole mass was heated on a water bath for 2 hours. The dark oil which separated out on cooling was mainly ethylxanthogenic acid p-methoxyphenyl ester, which was separated off and immediately treated with an alcoholic solution of caustic potash (19 g in 500 ml) at 80-90° for 2 hours. The main reaction which took place was:

$$C_2H_5O-C\overset{*}{S}-\overset{*}{S}-C_6H_4OCH_3 \xrightarrow{KOH} CH_3OC_6H_4\overset{*}{S}K + C\overset{*}{O}S + C_2H_5OH.$$

Together with formation of labeled potassium mercaptide there evolved radioactive carbonyl sulfide. In this connection, the decomposition reaction of the ester was carried out in a sealed apparatus with removal and absorption of carbonyl sulfide with alcoholic KOH solution.

After the main bulk of alcohol had been driven off, into the reaction mixture was run dilute sulfuric acid (1:7) until an acid reaction was obtained with Congo red; the resulting mercaptan was separated off and steam-distilled. For prevention of oxidation of the mercaptan to the disulfide, sulfuric acid (1:7) and about 10 g of zinc dust were added to the distillation flask. The distillate was extracted with ether, the ethereal extract was dried with fused calcium chloride and after the ether had been driven off, the remaining p-methoxythiophenol was vacuum-distilled. The fraction was collected which had b. p. 89-90° (4-5 mm). The yield was about 70%.

p-Biphenylmercaptan-S^{35} was prepared via the diazo compound and the biphenyl ester of labeled ethylxanthogenic acid was prepared similarly to the synthesis of labeled p-methoxythiophenol. The diazo compound, prepared from p-biphenylamine (30 g), reacted with the labeled potassium ethylxanthate (53 g) under the above-described conditions. Ethylxanthic acid biphenyl ester, $C_2H_5O-CS^*-S^*-C_6H_4C_6H_5$, obtained as a dark oil, was separated from the reaction mixture and immediately treated with an alcoholic solution of alkali (20 g KOH in 500 ml alcohol) under the same conditions as in the case of p-methoxyphenyl ester.

The precipitate which remained after the alcohol was driven off was mainly biphenyl disulfide. To this precipitate was added dilute sulfuric acid (1:7) and zinc dust (10-15 g); the whole mass was boiled for 2-3 hours under reflux and then was steam-distilled. The steam-distilled biphenylmercaptan-S^{35} congealed in the form of lustrous white flakes which were filtered off, recrystallized 2 times from alcohol and dried in a vacuum-desiccator over calcium chloride. The resulting product had m. p. 109°. Yield ~ 70%.

Diethyl disulfide-S^{35} was synthesized from ethyl iodide and radioactive sodium disulfide. Metallic sodium (5.8 g) was dissolved in ethyl alcohol (100 ml) and the solution was divided into two equal portions in volume. One portion was saturated with hydrogen sulfide until NaSH formed. The excess of hydrogen sulfide was removed by nitrogen. To this solution was added a second portion of sodium solution in alcohol and sodium sulfide formed. To the sodium sulfide in the flask fitted with reflux condenser was added crystalline radioactive sulfur (4 g) with a total activity of 1-3 m Cu and the whole mixture was heated on a water bath for 3-5 hours until complete solution of sulfur. All operations in the preparation of sodium disulfide, including the last stage, were carried out in a nitrogen atmosphere. 39.3 g ethyl iodide was carefully added with stirring to the cooled solution of radioactive sodium disulfide and the whole mass was heated for 1-2 hours on a water bath. On cooling, the reaction mixture was poured in water (~1 liter); diethyl disulfide separated out in the form of an oil; it was extracted with ether; the ethereal extract was dried with calcium chloride and after the ether was driven off, the product

was vacuum-distilled; b. p. 47.5-48° (10 mm), n_D^{20} 1.50687.

The specific activity of the obtained diethyl disulfide was half the specific activity of the initial sulfur.

n-Dibutyl disulfide-S^{35} was synthesized from n-butyl bromide and radioactive sodium disulfide in the same manner as diethyl disulfide. The product was purified by distillation with collection of the fraction 228-229°. The yield was almost quantitative.

Dibenzyl disulfide-S^{35} was synthesized from benzyl chloride and radioactive sodium disulfide according to a method similar to the synthesis of diethyl disulfide. After pouring the reaction mass in water, the product separated out as white lustrous crystals which were filtered off and recrystallized twice from alcohol to constant m. p. 77°. Yield ~ 80%. The specific activity of the sulfur in the product was equal to half of the specific activity of the initial sulfur.

p, p'-Dinitrodiphenyl disulfide-S^{35} was previously described in the literature [7]. We synthesized dinitrodiphenyl disulfide from p-chloronitrobenzene and radioactive sodium disulfide by a method similar to that previously described. The product separated out as a mixture of three crystalline forms. For our work we separated the form with m. p. 179°. Yield 40-50%.

Diphenyl disulfide-S^{35} was synthesized from bromobenzene and radioactive sulfur monochloride via the organomagnesium compound [5]. On reacting bromobenzene (60 g) with magnesium filings (9 g) in absolute ether (100 ml), we prepared phenylmagnesium bromide. Into the resulting solution of this compound with stirring and cooling was run a solution of radioactive sulfur monochloride (26.5 g) in ether (35 ml). The radioactive sulfur monochloride was prepared by the exchange reaction of S_2Cl_2 with radioactive elementary sulfur. For this purpose, to the S_2Cl_2 was added a small amount (0.01-0.05 g) of sulfur with an activity of 1-3 m Cu; the mixture was set aside overnight and then distilled, the fraction being collected with b. p. 137-138°. After addition of $S^*{}_2Cl_2$ to the organomagnesium compound, the resulting complex was decomposed in the cold with ice water and acidified with hydrochloric acid. The diphenyl disulfide which formed together with other products was extracted with ether, the ethereal extract was dried with fused calcium chloride and after driving off the ether, it was vacuum-distilled. The fraction collected had b. p. 190-195° (10 mm). After recrystallization from alcohol, the labeled diphenyl disulfide with m. p. 60.5° was obtained. Yield ~ 30%.

Together with diphenyl disulfide, this synthesis yielded labeled diphenyl monosulfide, which distilled off in vacuum before the disulfide.

Di-p-tolyl disulfide-S^{35} was prepared by oxidizing the labeled thiocresol with potassium ferricyanide [8]. Thiocresol-S^{35} (12.5 g) prepared previously, was dissolved in alkali (20%); the solution was heated and into it was run a hot solution (41 g) of potassium ferricyanide in water (60 ml); ditolyl disulfide separated out. On cooling, the product was filtered off, dried in a vacuum-desiccator over calcium chloride, dissolved in benzene, and the benzene solution was treated with caustic soda solution (5%) to remove possibly admixed thiocresol. After evaporation of benzene in the cold, ditolyl disulfide was recrystallized twice from methyl alcohol to constant m. p. 46°.

Di-p-methoxydiphenyl disulfide-S^{35} was prepared by oxidation of labeled p-methoxythiophenol with potassium ferricyanide. For this purpose, methoxythiophenol-S^{35}, synthesized previously (22 g), was dissolved in 20% alkali solution and to the warmed solution was added a hot solution of potassium ferricyanide (95 g) in water (150 ml). After mixing, the reaction mass was heated for 10-15 minutes more and after cooling, the white crystals of p-methoxydiphenyl disulfide-S^{35} which separated out were filtered off and recrystallized from ethyl alcohol; m. p. 44°.

Di-p-biphenyl disulfide-S^{35} was synthesized by oxidation of labeled biphenylmercaptan with potassium ferricyanide also, as was done in the case of the previous two compounds. Also, labeled biphenyl disulfide was prepared indirectly in the synthesis of labeled biphenylmercaptan. After decomposition of the biphenyl ester of labeled ethylxanthic acid with alcoholic alkali solution, together with the mercaptan was formed the disulfide, which was separated off and purified by recrystallization from large volumes of alcohol or from dioxane. The resulting product had m. p. 149-149.5°.

SUMMARY

Synthesis methods were developed and the following compounds, labeled with the radioactive sulfur isotope S^{35}, were synthesized: butyl mercaptan, benzyl mercaptan, p-thiocresol, p-methoxythiophenol, biphenyl mercaptan, potassium ethyl xanthate, diethyl disulfide, n-dibutyl disulfide, dibenzyl disulfide, p, p'-dinitrodiphenyl disulfide, diphenyl disulfide, di-p-tolyl disulfide, di-p-methoxydiphenyl disulfide and di-p-biphenyl disulfide.

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CATALYTIC TRANSFORMATIONS OF AMINES OVER ALUMINOMOLYBDENUM CATALYST

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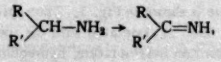
In the presence of a number of catalysts, mainly metallic in nature (Ni, Cu, Pt, Pd, Co, Ag), and at temperatures above 300° the primary aliphatic amines suffer dehydrogenation; here the primary amines with the amino group attached to a primary carbon atom are converted into nitriles [1]. The reaction proceeds through the stage of forming the aldimine RCH = NH [2]. Secondary and tertiary amines (with the amino group attached to primary carbon atoms) are also converted into nitriles with the simultaneous formation of olefins [1], for example: $(C_5H_{11})_2NH \rightarrow C_5H_{10} + C_4H_9CN + 2H_2$.

Primary amines, where the amino group is attached to a secondary carbon atom, are dehydrogenated only to the ketimine stage [2, 3]:



which can then suffer a number of secondary condensation reactions.

At temperatures below 300° in the presence of the same catalysts the main reactions are the disproportionation and desamination of the amines with the formation of a mixture of various amounts of primary, secondary and tertiary amines, olefins and ammonia. At higher temperatures the same reactions accompany the dehydrogenation reaction to a greater or lesser degree. Here the secondary desamination reaction plays an especially substantial part, as the result of which in the presence of certain catalysts, mainly nonmetallic in nature (Al_2O_3, $ZnCl_2$, etc.), the amines show complete decomposition into olefins and ammonia.

In the present study we investigated the behavior of a number of amines on an aluminomolybdenum oxide catalyst (molybdenum oxide deposited on aluminum oxide), in the presence of which the reactions of hydrogenation, dehydrogenation, cracking, hydration and dehydration can proceed. As study subjects we selected amines of diverse structure: n-propylamine, di-n-propylamine, isopropylamine and cyclopentylamine. The starting isopropylamine, n-propylamine and cyclopentylamine were obtained by the respective reductive amination of acetone, propionaldehyde and cyclopentanone with ammonia under H_2 pressure in the presence of skeletal nickel. The catalytic amination of the enumerated carbonyl compounds under pressure gives better yields than does catalytic amination at atmospheric pressure (especially in the preparation of cyclopentylamine) [4], and this method can be recommended as being preparative.

When n-propylamine, isopropylamine and di-n-propylamine were passed over an aluminomolybdenum catalyst at temperatures below 400° the predominant reaction was disproportionation of the amines with the formation of a mixture of primary, secondary and tertiary amines, olefins and ammonia by the schemes:

$$2C_3H_7NH_2 \rightleftarrows NH_3 + (C_3H_7)_2NH,$$

$$(C_3H_7)_2NH + C_3H_7NH_2 \rightleftarrows (C_3H_7)_3N + NH_3,$$

$$C_3H_7NH_2 \rightarrow C_3H_6 + NH_3 \text{ etc.}$$

At temperatures above 400° gas formation showed considerable increase and the catalyzate no longer contained the original amine; here considerable differences in the behavior of amines differing in structure was observed.

At temperatures above 400° the n-propylamine begins to show considerable dehydrogenation with the formation of propionitrile. At temperatures around 500° the formed propionitrile suffers partial decomposition, giving acetonitrile. Thus, at 490° the catalyzate is practically devoid of the original amine and consists of a mixture of acetonitrile (67%) and propionitrile (33%) with trace amounts of secondary and tertiary amines as impurities. Special experimental studies made on the behavior of propionitrile over the same catalyst confirmed the fact that the acetonitrile is formed specifically as the result of propionitrile decomposition.

At 500° the di-n-propylamine behaves in the same manner as the n-propylamine; however, in this case there is very strong gas formation and only a small amount of liquid catalyzate was collected, containing acetonitrile (14%) and propionitrile (86%). The escaping gases contain a large amount of saturated hydrocarbons.

Of special interest are the catalytic transformations of isopropylamine. At temperatures above 400° it also suffers considerable dehydrogenation. However, in the presence of the aluminomolybdenum catalyst, in contrast to metallic catalysts, the dehydrogenation fails to stop at the ketimine stage, and instead is accompanied by cracking, which leads to the formation of acetonitrile (at 500° the yield is 10%). At the same time the deamination rate for the isopropylamine shows a sharp increase; at 500° more than half of the passed amine is deaminated by the reaction: $C_3H_7NH_2 \rightarrow C_3H_6 + NH_3$, with the formation of ammonia (57 mole %), propylene (32 mole %), and the hydrogenation and cracking products of the latter – saturated hydrocarbons (31 mole %). The catalyzate contains only trace amounts of secondary and tertiary amines.

Even more conclusive results are obtained if, to suppress the deamination reaction, the isopropylamine is passed over the catalyst in a stream of ammonia. Under these conditions up to 50% of the starting isopropylamine is converted into acetonitrile. The curve giving the relationship between the yield of acetonitrile from isopropylamine and the reaction temperature is shown in Fig. 1. The rapid decrease in the acetonitrile yield, occurring as temperature is raised above 500°, is associated with the increase in the rate of a number of side reactions, mainly the reactions of isopropylamine deamination, hydrogenation and cracking of acetonitrile [5]. This is indicated by the change in the composition of the escaping gases with temperature (Fig. 2).

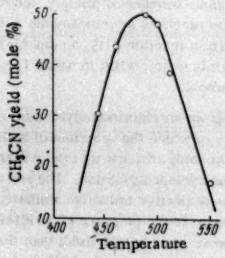


Fig. 1. The formation of acetonitrile with passage of isopropylamine over aluminomolybdenum catalyst.

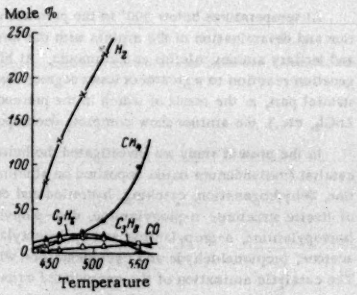


Fig. 2. Composition of the gaseous reaction products obtained in the passage of isopropylamine over aluminomolybdenum catalyst (in mole % on the isopropylamine passed).

It can be seen that the formation of acetonitrile from isopropylamine proceeds through the stage of amine dehydrogenation to the ketimine and the decomposition of the latter with the formation of acetonitrile:

TABLE 1

Transformations of Amines Over Aluminomolybdenum Catalyst

Temperature	Amine passed (in g)	Rate of passage ml/hr.	Rate of passage ml/ml of catalyst/hr.	Yield of liquid catalyzate (g)	Yield of liquid catalyzate (%)	Yield of CH_3CN (g)	Yield of CH_3CN (mole %)	Formed CN′ (mole · 10^{-4})	Formed CN′ (mole %)	Formed NH_3 (mole · 10^{-4})	Formed NH_3 (mole %)	Gas formed (minus NH_3) (in liters)
Di-n-propylamine												
300°	13.2	—	0.7	11.7a	89	0	0	—	—	—	—	0.85
400	7.8	—	0.3	4.0b	51	0	0	—	—	11	14	3.50
500	5.8	—	0.2	0.6c	11	—	—	0.18	0.3	11	19	4.25
n-Propylamine (in stream of NH_3)												
490	11.2	—	—	8.0d	72	—	—	8.0	4.6	—	—	11.4
Isopropylamine												
400	7.7	—	0.26	2.0e	26	0	0	0.03	0.02	78		2.52
500	10.4	—	0.22	1.8f	17	1.1	10	0.04	0.02	100	57	7.38
Isopropylamine (in stream of NH_3)												
446	11.2	5.2	—	—g	—	2.82	30.4	1.8	1.0	—	—	5.05
462	11.0	5.3	—	—g	—	3.95	43.4	5.3	2.9	—	—	7.9
489	11.4	5.35	—	—g	—	4.64	49.7	6.5	3.4	—	—	11.4
501	10.3	5.0	—	—g	—	4.04	47.7	9.2	5.3	—	—	—
513	10.6	5.1	—	—g	—	3.34	38.3	14.4	8.0	—	—	13.7
551	11.5	5.4	—	—g	—	1.63	17.2	—	—	—	—	24.9
Cyclopentylamine (in stream of NH_3)												
484	18.8	6.6	—	6.0h	91	0	0	0	0	—	—	15.8
500	18.2	6.6	—	5.0h	76	0	0	0	0	—	—	14.0

Notes. Composition of liquid catalyzate: a) primary, secondary and tertiary amine and traces of propionitrile; b) secondary and tertiary amines, propionitrile, traces of primary amine; c) 14% CH_3CN and 86% C_2H_5CN; traces of secondary and tertiary amines; d) 67% CH_3CN and 33% C_2H_5CN; traces of secondary and tertiary amines; e) primary, secondary and tertiary amines, small amount of ketimine; f) 60% CH_3CN; remainder — secondary and tertiary amines; g) CH_3CN; quantity after distillation see in column "Yield of CH_3CN"; h) about 70% of catalyzate — cyclopentene in mixture with cyclopentane and cyclopentadiene; about 30% of catalyzate — initial cyclopentylamine in mixture with corresponding secondary amine.

TABLE 2

Composition of Escaping Gases (minus NH_3) upon Passage of Amines Over Aluminomolybdenum Catalyst

Temperature	Quantity of gas formed (in liters)	Composition of gas (in vol. %)						Ratio to amine passed (in mol. %)				
		C_nH_{2n}	CO*	H_2	N_2**	C_nH_{2n+2}	where n	C_nH_{2n}	CO	H_2	N_2	C_nH_{2n+2}
Di-n-propylamine												
300°	0.85	1.1	0.5	44.8	—	5.0	—	9.3	0.1	12.2	—	1.4
400	3.50	6.0	0.5	61.2	—	11.2	—	11.4	1.0	116	—	21.3
500	4.25	6.6	8.5	53.2	—	31.3	—	—	—	—	—	—
n-Propylamine (in stream of NH_3)												
490	11.4	1.6	2.2	87.5	0.7	8.1	1.53	4.0	5.8	219	1.8	20.3
Isopropylamine												
400	2.52	20.9	0	51.2	—	12.3	—	16.7	0	40.9	—	9.8
500	7.38	18.2	4.5	45.3	—	17.5	—	31.7	7.7	79 0	—	30.5
Isopropylamine (in stream of NH_3)												
446	5 05	13 1	1.6	71.3	0.2	13.9	2.05	14.0	1.8	79	0.2	15.4
462	7.9	10.6	1.9	72.5	1.0	14.1	2.08	18.6	3.3	127	1.8	24.8
489	11.4	7.5	2.4	72.6	1.4	16.1	1.72	18.6	5.9	180	3.5	39.8
513	13.7	6.0	2.3	70.7	5.1	15.9	1.59	19.1	7.3	225	16.2	50.6
551	24.9	0.5	1.5	57.9	19.8	20.5	1.19	2.7	8.0	308	105	109

* Formed due to partial, additional reduction of catalyst.

** Formed together with part of H_2 due to decomposition of ammonia in accord with reaction: $2NH_3 \rightarrow N_2 + 3H_2$.

As a result, in this case also, the same as for n-propylamine, the end reaction product is the one that shows the greatest thermodynamic stability under these conditions, namely acetonitrile.

Cyclopentylamine, in which, the same as for isopropylamine, the NH group is found attached to a secondary carbon atom, however, behaves differently than does isopropylamine. Here the main direction of the reactions (even with passage of the amine in a stream of ammonia) is desamination with the formation of cyclopentene, and also cracking with the formation of large volumes of gaseous reaction products. The cyclopentene that is formed under these conditions is partially hydrogenated to cyclopentane and also shows disproportionation into cyclopentane and cyclopentadiene [6]. We were unable to show the presence of nitriles in the reaction products. The difference in the behavior of cyclopentylamine and isopropylamine under the same conditions is evidently associated with the greater ease of cleavage of the elements of ammonia to give a cyclic olefin – cyclopentene, when compared with the formation of an aliphatic olefin – propylene.

EXPERIMENTAL

Synthesis of amines. A mixture of 348 g (6 moles) acetone and 550 g 37% aqueous ammonia solution (12 moles) was hydrogenated in an autoclave in the presence of 35 g skeletal nickel catalyst at 90-100° and under a hydrogen pressure of 50-76 atm. When absorption of hydrogen was complete, the catalyst was filtered off and from a Favorsky flask was driven off the fraction boiling up to 50°, after which the obtained amine was distilled on a column (with glass packing) with an efficiency of 37 theoretical plates. Yield of isopropylamine was 172 g (49%):

B.p. 31.3° (740 mm), n_D^{15} 1.3770, d_4^{15} 0.6931. Literature data give [7, 8]: b.p. 31.5° (743 mm), $n_D^{15.4}$ 1.37698, $d_4^{15.4}$ 0.6935.

n-Propylamine was prepared similarly from propionaldehyde; yield 30%:

B.p. 46.5-46.6° (744 mm), d_4^{20} 0.7149, n_D^{20} 1.3910. Literature data give [8, 9]: b.p. 47.8° (760 mm), $d_4^{15.5}$ 0.7209, $n_D^{15.6}$ 1.39006, d_4^{20} 0.7155.

For the preparation of cyclopentylamine, in the autoclave was placed 200 g cyclopentanone, 360 ml (saturated at 0°) aqueous ammonia solution and 20 g skeletal nickel catalyst. Hydrogenation was carried out under a hydrogen pressure of 120-130 atm, at a temperature of 50-60°. The catalyst was filtered off and the catalyzate was boiled for 2 hours under reflux to remove the excess ammonia. Then, to separate the amine from aqueous solution was added caustic potash, the amine was separated off, dried and distilled on a column with an efficiency of 35 theoretical plates. Yield of cyclopentylamine was 97.1 g (50%):

B.p. 108.2° (760 mm), n_D^{20} 1.4511, d_4^{20} 0.8683. Literature data give [10]: b.p. 108-109° (767 mm), n_D^{20} 1.4515, d_4^{20} 0.8689.

To investigate the catalytic transformations, previously distilled commercial di-n-propylamine, b.p. 109°, d_4^{20} 0.7385, n_D^{20} 1.4045, was used.

Conditions of catalytic experiments. Catalytic experiments were carried out in a flow system. The aluminomolybdenum catalyst was prepared by impregnation of grains of aluminum oxide with an ammoniacal solution of ammonium molybdate and contained 14.9% by wt. of MoO_3 and 85.1% Al_2O_3 (11 mol % MoO_3 and 89 mol. % Al_2O_3). The impregnated catalyst was dried and slowly heated in a stream of air to 500°. Before each experiment, the catalyst was reduced in a stream of hydrogen at 500°. After the experiment, the catalyst was regenerated: the coke deposit was calcined by blowing in a stream of air at 500°.

The liquid catalyzate, collected in the receiver and in traps, was cooled to −20°, carefully heated under reflux for removal of dissolved ammonia, and then distilled. The corresponding fractions were analyzed for content of primary, secondary and tertiary amines and nitriles [11]. The quantity of cyanide ion which formed was determined by titration with $AgNO_3$ solution; the gaseous reaction products were liberated from ammonia and then analyzed on a VTI apparatus. The conditions and results of a number of experiments are given in Table 1; the composition of the outgoing gases are given in Table 2.

SUMMARY

1. The transformations of n-propylamine, di-n-propylamine, isopropylamine and cyclopentylamine on an aluminomolybdenum catalyst were studied.

2. It was shown that at temperatures below 400° there proceed mainly disproportionation reactions with the formation of mixtures of primary, secondary and tertiary amines.

3. At a temperature of 450-500° the isopropylamine suffers a previously unknown type of decomposition and dehydrogenation with the formation of acetonitrile. n-Propylamine and di-n-propylamine are dehydrogenated to propionitrile. At temperatures above 400° the desamination process increases in strength, and in the case of cyclopentylamine it appears as the predominant process.

4. The reductive amination of cyclopentanone in the presence of skeletal nickel catalyst can be recommended as a preparative method for obtaining cyclopentylamine.

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DEHYDRATION OF SUBSTANCES USING VACUUM AND DEEP FREEZING

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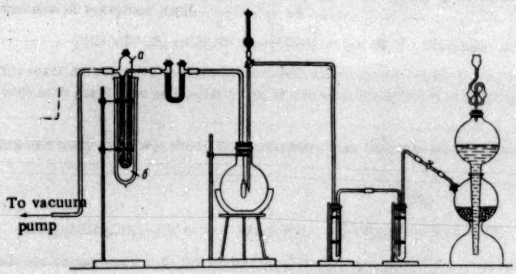
Certain substances, which contain in their composition water of crystallization (for example, salts of rare-earth elements with organic acids), upon being dried at a temperature exceeding 100°, undergo partial decomposition. At the same time, in order to dehydrate certain salts that firmly hold their water of crystallization, it is necessary to subject them to prolonged heating, higher temperatures or prolonged standing in vacuum at a correspondingly lowered temperature. A greater rate of dehydration is thus obtained under a higher vacuum.



Scheme of apparatus for dehydration of salts.

We found it difficult to dehydrate the d-camphor-β-sulfonates and *n*-bromo-d-camphor-p-sulfonates of individual rare-earth elements. Dehydration in vacuum during passage of a stream of dry hydrogen (pressure 5 mm, temperature 85-90°) went very slowly (over 20 hours).

This circumstance led us to employ deep freezing of the receiver (filled with calcium chloride) during the vacuum-drying, which lowered the vapor pressure of the H_2O which was removed from the drying zone by the stream of dry hydrogen passed through the capillary.

For this we used the following apparatus. In a round-bottomed flask, heated with boiling water, was placed several weighed portions of the salts located in small open test-tubes fitted with ground stoppers. The flask was closed with a rubber stopper with two outlet tubes; one of them reaches almost to the bottom of the flask and its end is drawn out into a thin capillary. A slow stream of dry hydrogen is introduced into the flask through the capillary.

A specially prepared glass column a, filled with calcium chloride and lowered inside a Dewar flask b with liquid air served as the receiver for the condensed water. The outlet tubes of the calcium chloride column join it with a flask from one side and with the oil pump from the other.

For complete dehydration of salts, in our case, it proved sufficient to heat for 2 hours at 85-90° under a pressure of 8-10 mm. The liquid air may be replaced by a solution of dry ice in acetone.

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THE SYNTHESIS OF ACETYLENES BY EXHAUSTIVE METHYLATION

Ya.M. Slobodin and N.A. Selezneva

The decomposition of fully substituted ammonium bases is used for the synthesis of compounds that contain either one or several double bonds [1,2].

We had established [3] that the exhaustive methylation of dimethylpiperideine leads to the formation of pyrylene – a hydrocarbon that contains a conjugated acetylene-ethylene system of bonds. This study showed for the first time the possibility of forming the acetylene bond in the thermal decomposition of fully substituted ammonium bases. It could be assumed that the thermal decomposition of ethylene bis(trimethylammonium hydroxide) will lead to the formation of acetylene itself:

$$\left[(CH_3)_3\overset{+}{N}CH_2 - CH_2\overset{+}{N}(CH_3)_3\right](OH)_2^- \rightarrow CH \equiv CH + 2N(CH_3)_3 + 2H_2O.$$

Actually, when this reaction was run a gaseous hydrocarbon was obtained, which proved to be pure acetylene. The reaction proceeds with such great ease and rapidity that it can be recommended as a demonstration experiment.

In the above mentioned study [3] it was shown that quaternary ammonium bases, containing the unsaturated radicals

$$\left[(CH_3)_3\overset{+}{N}CH_2CH_2 - CH = C = CH_2\right] Y^-; \quad \left[(CH_3)_3\overset{+}{N}\overset{CH_2}{\overset{\|}{C}} - CH_2 - CH = CH_2\right] Y^-,$$

when distilled with alkali are decomposed with the formation of the same hydrocarbon, containing a conjugated acetylene-ethylene system of bonds. It was natural to expect that the thermal decomposition of unsaturated bis-ammonium bases of type

$$\left[(CH_3)_3\overset{+}{N} - \underset{R}{CH} - CH = CH - \underset{R}{CH} - \overset{+}{N}(CH_3)_3\right] (OH)_2^-$$

would also lead to the formation of enynes with conjugated bonds.

In the present study we subjected 1,4-dimethyl-2-butenylene bis(trimethylammonium hydroxide) to thermal decomposition. The starting material for its preparation was 2,4-hexadiene, which was converted into the dibromide when reacted with the calculated amount of bromine. Treatment of the dibromide with trimethylamine gave the diammonium salt in quantitative yield, which when distilled with a slight excess of alkali was decomposed with the formation of a hydrocarbon.

The hydrocarbon boiled at 88-89°. When hydrogenated it added 3 moles of hydrogen. It failed to react with reagents for monosubstituted acetylenes. The hydrocarbon showed considerable molecular refraction exaltation. The Raman spectrum of the hydrocarbon showed the presence of a group with frequencies of 1577, 1628, 1650, 1936, 2137 and 2222 cm^{-1}, characterizing the presence of a conjugated double and triple bond in the hydrocarbon. The frequencies 1628 and 1650 cm^{-1} show that the double bond in the conjugated system is not found at the end of the carbon chain. The frequency 1577 cm^{-1}, constantly present in conjugated enynes [4], supports the structure of the investigated hydrocarbon as being a conjugated enyne. The same should also be said of the frequency 1936 cm^{-1}, shown by us to be also present in other enynes [3]. The frequencies 2137 and 2222 cm^{-1} show that the hydrocarbon is a disubstituted acetylene. Combination of the obtained data shows that our investigated hydrocarbon is 2-hexen-4-yne.

Taking into consideration the easy availability at the present time of diene hydrocarbons with conjugated bonds, many of which are synthesized on a commercial scale, it is possible to make extensive use of them for the synthesis of enynes – a class of hydrocarbons that up to now have been quite difficultly available.

The general synthesis of enynes from conjugated dienes can be depicted by the scheme:

$$R{-}CH{=}CH{-}CH{=}CH{-}R \xrightarrow{Br_2} R{-}CHBr{-}CH{=}CH{-}CHBr{-}R \xrightarrow{N(CH_3)_3}$$

$$\longrightarrow \left[(CH_3)_3\overset{+}{N}{-}\underset{R}{CH}{-}CH{=}CH{-}\underset{R}{CH}{-}\overset{+}{N}(CH_3)_3\right]Br_2^- \xrightarrow{NaOH}$$

$$\longrightarrow R{-}C{\equiv}C{-}CH{=}CH{-}R + 2N(CH_3)_3 + 2H_2O + 2NaBr.$$

All of the phases of this process proceed with yields that are close to quantitative.

In a previous communication [3] it was mentioned, after treatment of a fully substituted ammonium base, containing an unsaturated radical, with silver oxide, that subsequent thermal decomposition fails to lead to the formation of a hydrocarbon. We observed a similar phenomenon in the present study.

A study of the reaction of silver nitrate with an aqueous solution from the receiver, containing a small amount of unsaturated amine, revealed that mixing of the solutions even in the cold led to almost instantaneous reduction of the silver nitrate. Here silver oxide is reduced to the metal. It can be assumed that this explains our above-mentioned unsuccessful attempts to obtain hydrocarbons.

EXPERIMENTAL

Synthesis of acetylene. The starting material was ethylene bromide which was sealed in an ampul with an excess of trimethylamine. The mixture was set aside at room temperature for 1 month. After opening the ampul and driving off the excess trimethylamine, the salt was washed with absolute ether and dried. Analysis of it showed a decreased nitrogen content. In connection with this, the salt was again sealed in a tube with excess trimethylamine and set aside at room temperature for 1 month more.

Found %: N 8.5, 8.77. $C_8H_{22}N_2Br_2$. Calculated %: N 9.15.

The salt was placed in a Wurtz flask to which was added 40% KOH solution, amounting to a 15-20% excess of the calculated quantity; slight evolution of heat and gas was noted. The flask was fitted with condenser and receiver. The gaseous reaction products were washed with water, sulfuric acid and passed into a gasometer, filled with saturated hydrochloric acid solution. Upon heating the flask, decomposition of the base proceeded vigorously and was complete after 10-15 minutes. Water and water-soluble amines were collected in the receiver.

The gaseous hydrocarbon reacted quantitatively with ammoniacal solutions of silver and monovalent copper to form the characteristic metallic derivatives of acetylene. Acetaldehyde was obtained by Kucherov's reaction. The yield of acetylene was about 80%.

Bromide of 2,5-bis-(trimethylammonium)-3-hexene. Into a flask fitted with stirrer and reflux condenser was placed a solution of hexadi-2,4-ene in carbon tetrachloride. On cooling to -10°, the calculated quantity of bromine, dissolved in carbon tetrachloride, was slowly run into the solution. The reaction products were washed with water, soda, again with water, dried over calcium chloride and distilled [5]. The yield of bromide was quantitative.

B.p. 66.5° at 2 mm, d_4^{20} 1.6216, n_D^{20} 1.5355.
Found %: Br 66.15. $C_6H_{10}Br_2$. Calculated %: Br 66.11.

To the solution (cooled with ice water) of hexadiene dibromide in ether or in benzene was added, with vigorous stirring, a solution of trimethylamine in the same solvent.

The reaction was complete after several hours. However, in preparing the analytically pure diammonium salt it was necessary to hold the mixture in a well-closed vessel for 10-15 days at room temperature. The precipitate was quickly filtered off and dried in a desiccator over alkali. Yield of salt was nearly quantitative.

Found %: N 7.65; Br 43.88. $C_{12}H_{22}N_2Br_2$. Calculated %: N 7.77; Br 44.44.

2-Hexen-4-yne. Into the diammonium salt in the Wurtz flask was run a 40% solution of KOH in 10% ex-

cess over the calculated quantity. The mixture was slowly distilled. When the distillation of water was almost complete, decomposition of the diammonium base began. There were two layers in the receiving flask. The hydrocarbon layer was separated off, washed with water, 10% sulfuric acid, again with water and dried over calcium chloride. The yield of hydrocarbon was 85%.

B.p. 88-89°, d_4^{20} 0.7710, n_D^{20} 1.4918, MR_D 30.09; calc. 27.38; exaltation 2.71.

Hydrogenation over platinum catalyst. Subst. 0.2794 g; H_2 226 ml(0°, 760 mm). C_6H_8FF. Calculated: H_2 234.7 ml.

Raman spectrum of hydrocarbon: 295(2), 361(1), 442(2), 791(1), 821(2), 938(3), 1095(5), 1150(7), 1186(7), 1239(5), 1290(5), 1344(4), 1393(4), 1444(3), 1577(2), 1628(20), 1650(20), 1936(8), 2137(4), 2222(4), 2860(4), 2921(5), 2980(5), 3076(2).

SUMMARY

1. It was established that the thermal decomposition of ethylene bis(trimethylammonium hydroxide) yields pure acetylene.

2. The thermal decomposition of 1,4-dimethyl-2-butenylene bis(trimethylammonium hydroxide) yields 2-hexen-4-yne.

3. The studied reaction can be a general method for the synthesis of enynes and the simpler acetylenes.

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THE REACTION OF TRIMETHYLAMINE WITH POLYHALIDES

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In previous communications it was shown that the thermal decomposition of ammonium bases can lead not only to the formation of compounds with double bonds, but also of acetylenes [1], enynes [1,2], and even of compounds of the cyclopropane series [3]. In this connection it was necessary to elucidate the conditions for the formation of the salts of polyammonium bases from polyhalides with variable halogen atom distribution in the carbon chain.

It is indicated in the literature that compounds containing 2 halogen atoms on one carbon, as, for example, in methylene iodide, are incapable of forming a stable diammonium salt [4]. In like manner for ethylene bromide only the salts of the monoammonium derivatives are known [5].

In this paper we describe the results of studying the reaction of trimethylamine with various halides; here it was established that the halogen atoms, found in the β-position to each other, fail to show substantial influence on their reaction with trimethylamine, while the halogen atoms on adjacent carbons do exert a substantial influence on this process. In the latter case the reaction proceeds in stepwise manner. Diprimary α-dibromides react more rapidly than do primary-secondary, and the latter react more rapidly than do the primary-tertiary. The yields of the diammonium salts in the first case are considerably higher than in the second and especially in the third case. Thus, ethylene bromide at room temperature showed reaction with trimethylamine to the extent of 95%, forming the diammonium salt, while propylene bromide in twice the time showed 50% reaction, and isobutylene bromide only 30%.

Halogen atoms found on the same carbon show a very strong influence on the reaction. Methylene iodide at room temperature showed reaction with trimethylamine to the extent of 95% in one month; however, the resulting product was a mixture, containing 51% of the monoammonium salt and 49% of the diammonium salt. In the same length of time bromoform formed only 50% salt, which proved to be practically pure triammonium salt. The formation of the tetraammonium salt from trimethylamine and 1,2,3,4-tetrabromobutane proceeds in stepwise manner and is complete in about 3 months.

A double bond in the β-position to the halogen atom sharply accelerates the reaction. Allyl bromide and crotyl chloride react very rapidly with trimethylamine. The reaction is practically ended about the time all of the trimethylamine has been added. The dibromides of conjugated dienes, containing 2 bromine atoms in β-positions to the double bond, react explosively with trimethylamine. This requires running the reaction in diluents (alcohol, ether, benzene) and with good cooling.

The introduction of a hydroxy group in the α-position to the halogen shows a retarding effect. Thus, trimethylene bromide reacts quantitatively with trimethylamine in several days, while glycerol α,α'-dibromohydrin forms the diammonium salt only after standing at room temperature for 2 months with excess trimethylamine, and glycerol α,α'-dichlorohydrin under the same conditions forms only the monoammonium salt. In contrast to the hydroxy group the keto group accelerates the process of forming ammonium salts. Symmetrical dibromoacetone forms the diammonium salt with sufficiently great rapidity.

The data obtained by us show that the reaction for the formation of polyammonium salts from trimethylamine and the corresponding polyhalides is influenced by the mutual distribution of the halogen atoms, their nature, the degree of substitution shown by the carbon attached to the halogen, and apparently by factors of a steric character.

It was already mentioned in previous communications [1,2,7] that the thermal decomposition of bisammon-

ium bases, the same as for monoammonium bases containing an unsaturated radical, fails to lead to the formation of compounds with allene bonds. Intramolecular rearrangements take place right at the moment of reaction, leading to the formation of compounds with either the acetylene or a conjugated diene bond. Bisammonium bases, showing a double bond in the carbon chain attached to two ammonium groups, under thermal decomposition form the acetylene-ethylene system of bonds. To develop these observations we studied in the present investigation the thermal decomposition of propylene bis-(trimethylammonium hydroxide), trimethylene bis-(trimethylammonium hydroxide), trimethylallylammonium hydroxide and (3-cyanopropyl)trimethylammonium hydroxide.

It was experimentally established by us that the thermal decomposition of propylene bis-(trimethylammonium hydroxide), as could be expected, gives allylene in up to 90% yield. In the thermal decomposition of trimethylene bis-(trimethylammonium hydroxide) the predominant formation of allene could have been expected; however, a study of the gaseous thermal decomposition products revealed that in this case also allylene was formed in up to 85% yield. Closely similar results were also obtained in the thermal decomposition of trimethylallylammonium hydroxide. Here the only gaseous thermal decomposition product was allylene, but its yield was only 56%. Liquid products were obtained together with the allylene, showing a wide boiling range (60-137°) and containing unsaturated amines, and possibly allyl alcohol. In addition, these experiments permit assuming that the decomposition of trimethylene bis-(trimethylammonium hydroxide) under heating proceeds with the simultaneous elimination of trimethylamine from both quaternary ammonium groups without the formation of the intermediate trimethylallylammonium ion.

In the thermal decomposition of (3-cyanopropyl)trimethylammonium hydroxide there proceeded simultaneous saponification of the nitrile group and elimination of trimethylamine. An acid was obtained as a result, which showed a somewhat lower melting point than crotonic acid. Its mixed melting point with crotonic acid failed to be depressed. Consequently, here also rearrangement took place, as a result of which a compound with a conjugated system of bonds was formed.

EXPERIMENTAL

To prepare the salts, the halides were sealed in an ampul with a two-fold,with respect to the theoretical, quantity of trimethylamine. The mixture was set aside at room temperature, After definite intervals of time had elapsed, the ampuls were opened. The excess of trimethylamine was driven off. The salt was washed on a filter with ether, dried in vacuum and analyzed. Incase of incomplete reaction, the salt was again sealed with an excess of trimethylamine.

Methylene bis-(trimethylammonium iodide). The reaction of methylene iodide with trimethylamine at first proceeded rapidly. It was necessary to cool the mixture. After a month, the ampul was opened. The salt was difficultly soluble in alcohol and insoluble in ether. Analysis gave a reduced nitrogen content, which corresponded to a mixture of 51% mono- and 49% diammonium salt. Yield of salt was 95%.

Found %: N 5.8, 5.7. $C_7H_{20}N_2I_2$. Calculated %: N 7.26. $C_4H_{11}I_2N$. Calculated %: N 4.3.

Methylene tri-(trimethylammonium bromide). The initial stage of reaction of bromoform with trimethylamine proceeds with evolution of heat. The ampul was opened after a month. The salt was but slightly hygroscopic. It dissolved slowly in alcohol; it was insoluble in ether. Yield 50%.

Found %: N 10.0, 9.87. $C_{10}H_{28}N_3Br_3$. Calculated %: N 9.77.

Ethylene bis-(trimethyl ammonium bromide). The reaction between ethylene bromide and trimethylamine proceeded sluggishly. The ampul was opened after a month. Analysis showed a reduced nitrogen content. The precipitate was again sealed with an excess of trimethylamine and the mixture was again set aside for a month. The resulting product was hygroscopic. The yield was above 90%.

Found %: N 8.50, 8.77. $C_8H_{22}N_2Br_2$. Calculated %: N 9.15.

Cyclohexane-1,2-bis(trimethylammonium bromide). The reaction between cyclohexene bromide and trimethylamine proceeded very slowly. After only 3 months, formation of precipitate ceased. The yield was almost quantitative.

Found %: N 7.90, 8.00. $C_{12}H_{28}N_2Br_2$. Calculated %: N 7.78.

Propylene bis(trimethylammonium bromide). The reaction between propylene bromide and trimethylamine proceeded very slowly. The formation of crystals of the ammonium salt began only after a month had elapsed. The ampul was opened after 4 months. The salt was hygroscopic. Yield about 50%.

Found %: N 8.52, 8.65. $C_9H_{22}N_2Br_2$. Calculated %: N 8.75.

Isobutylene bis(trimethylammonium bromide). The reaction between isobutylene bromide and trimethylamine proceeded very slowly. The ampul was opened after 4 months. The salt was hygroscopic. Yield about 30%.

Found %: N 8.50, 8.25. $C_{10}H_{24}N_2Br_2$. Calculated %: N 8.38.

Trimethylene bis(trimethylammonium bromide). Trimethylene bromide was sealed in an ampul with trimethylamine. The formation of the bis-ammonium salt was complete after several days. Yield was near theoretical.

Found %: N 8.58. $C_9H_{24}N_2Br_2$. Calculated %: N 8.75.

Glyceryl(trimethylammonium bromide). Glycerol tribromohydrin was sealed in an ampul with trimethylamine. Formation of crystals of the ammonium salt took place slowly. The ampul was opened after 2 months. Analysis showed that the diammonium salt formed. The yield was almost quantitative.

Found %: N 6.87, 6.94. $C_9H_{22}N_2Br_2$. Calculated %: N 7.01.

The diammonium salt was again sealed with an excess of trimethylamine (three-fold) and set aside for 3 months. The resulting salt was slightly hygroscopic, slowly dissolved in water, and was difficultly soluble in alcohol. The yield was almost quantitative.

Found %: N 9.25, 9.07. $C_{12}H_{32}N_2Br_2$. Calculated %: N 9.16.

2-Methylpropenyl(trimethylammonium bromide). 1,2,3-Tribromoisobutane was sealed with an excess of trimethylamine. The crystalline precipitate began to appear only after a month had elapsed. The ampul was opened after 3 months. The salt was hygroscopic, readily soluble in water, somewhat less soluble in alcohol. It was the diammonium salt. The yield was quantitative.

Found %: N 7.01, 6.87. $C_{10}H_{26}N_2Br_2$. Calculated %: N 6.78.

The diammonium salt was sealed with a three-fold excess of trimethylamine. The mixture was set aside for 3 months. The salt was hygroscopic. The yield was quantitative.

Found %: N 8.78, 8.95. $C_{19}H_{34}N_3Br_3$. Calculated %: N 8.90.

Divinyl tetra(trimethylammonium bromide). The crystalline divinyl tetrabromide was sealed in an ampul with a two-fold excess of trimethylamine. The ampul was opened after 2 months. The resulting salt was a mixture of products. The salt was again sealed with a two-fold excess of trimethylamine and set aside for another month. The salt was slightly hygroscopic, readily soluble in water. Yield was close to quantitative.

Found %: N 9.36, 9.39. $C_{16}H_{38}N_4Br_4$. Calculated %: N 9.1.

Propan-2-ol-1,3-bis(trimethylammonium bromide)[6]. Glycerol dibromohydrin was sealed in an ampul with a two-fold excess of trimethylamine. After only several days, a precipitate of salt appeared. The reaction was complete after only 2 months. The salt was very hygroscopic. The yield was quantitative.

Found %: N 8.05, 8.09. $C_9H_{24}ON_2Br_2$. Calculated %: N 8.32.

3-Chloropropan-2-ol-1-trimethyl-3-ammonium chloride. Glycerol dichlorohydrin was sealed in an ampul with a two-fold excess of trimethylamine. The mixture was set aside for 3 months. The crystals of the salt started to come down only after a month of standing. Analysis showed that the salt was a mixture of approximately 80% monoammonium salt and 20% diammonium salt. The salt was recrystallized from alcohol.

Found %: N 7.38. $C_6H_{15}NCl_2$. Calculated %: N 7.45.

Propan-2-one-1,3-bis(trimethylammonium bromide). Symmetrical dibromoacetone was sealed with a two-fold excess of trimethylamine. The reaction proceeded with evolution of heat and after only 20-30 minutes, a precipitate of salt appeared. The ampul was opened after several days. The salt was very hygroscopic and yellowish in color. It had a pungent odor.

Found %: N 8.23, 8.28. $C_9H_{22}ON_2Br_2$. Calculated %: N 8.38.

(3-Cyanopropyl)trimethylammonium chloride. γ-Chlorobutyronitrile was treated with a two-fold excess of trimethylamine. The ampul was opened after 2 months. The salt was slightly hygroscopic. It was readily soluble in water.

Found %: N 15.8, 16.4. $C_7H_{13}N_2Cl$. Calculated %: N 17.23.

Trimethylallylammonium iodide. To allyl iodide was slowly added trimethylamine with intense cooling (-25°). The reaction evolved heat. The salt was analyzed after several days.

Found %: N 7.48, 7.62. $C_6H_{14}NBr$. Calculated %: N 7.77.

Trimethylcrotylammonium chloride. The reaction between crotyl chloride and trimethylamine in a sealed ampul proceeded rapidly and was practically complete after 40 hours. Chlorine was determined in the salt by titration.

Found %: Cl 23.71. $C_7H_{16}NCl$. Calculated %: Cl 23.74.

Divinyl-1,4-bis(trimethylammonium bromide)[8]. Into an ethereal solution of divinyl dibromide was slowly run cooled trimethylamine. The reaction was practically complete after several minutes. Without solvent and with insufficient cooling, the contents of the tubes were thrown out. The yield was quantitative.

Found %: Br (ionic) 47.95. $C_{10}H_{24}N_2Br_2$. Calculated %: Br 48.22.

3-Hexene-2,5-bis(trimethylammonium bromide). The reaction between 2,5-dibromo-3-hexene and trimethylamine went very vigorously and necessitated change of diluent (ether, benzene). The reaction was carried out in a flask fitted with stirrer. The mixture was well sealed and set aside at room temperature for several days. The yield was quantitative.

Found %: N 7.65; Br 43.88. $C_{12}H_{28}N_2Br_2$. Calculated %: N 7.77; Br 44.44.

Thermal decomposition of propylene bis(trimethylammonium hydroxide), trimethylene bis(trimethylammonium hydroxide) and trimethylallylammonium hydroxide. The ammonium salt was placed in a Wurtz flask, into which was run 40% KOH solution, amounting to a 10% excess over the calculated quantity. The flask was slowly heated. Evolution of gas was noted even at the start of heating. The gas was washed with water, weak sulfuric acid and was collected in a gasometer. The total content of unsaturated compounds in the gas was determined by absorption of bromine water; content of allylene was determined by absorption with an ammoniacal solution of silver oxide. Trimethylallylammonium hydroxide decomposition products were salted out with potash. The upper layer was separated off, dried and distilled. It boiled in a wide range (60-137°). With ammoniacal silver oxide solution in the cold it gave a silver mirror, indicating an unsaturated tertiary amine [3].

The yields of allylene (in %) on decomposition of hydroxides: propylene bis(trimethylammonium hydroxide), 90, trimethylene bis (trimethylammonium hydroxide), 85, trimethylallylammonium hydroxide, 56%.

Decomposition of (3-cyanopropyl)trimethylammonium hydroxide. (3-cyanopropyl)trimethylammonium chloride was placed in a Wurtz flask, to which was added a small (40%) excess of alkali. The flask was heated on a small flame. Water and the decomposition products were collected in a receiver. On completion of distillation, the contents of the Wurtz flask were dissolved in water, acidified with sulfuric acid and extracted with ether. After evaporation of the ether, a crystalline acid remained with m.p. 60°, which after crystallization from alcohol, had m.p. 68°. A mixed sample of this acid with crotonic acid melted without depression (68-70°).

SUMMARY

1. Twenty ammonium salts were prepared from trimethylamine and halogenated derivatives, differing in the number of halogen atoms, their mutual arrangement, and the degree of substitution shown by the halogen-containing carbon.

2. It was shown that the thermal decomposition of propylene bis- and trimethylene bis(trimethylammonium hydroxide) gives allylene in 85-90% yields. Trimethylallylammonium hydroxide also shows decomposition with the formation of allylene, but here the yields are considerably lower (56%). We were unable to show the presence of allene in any of these cases.

3. As the result of rearrangement, crotonic acid is formed in the thermal decomposition of (3-cyanopropyl) trimethylammonium hydroxide.

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OZONIZATION OF UNSATURATED COMPOUNDS

II. A STUDY OF THE CURVES FOR THE ABSORPTION OF OZONE BY UNSATURATED COMPOUNDS AND THEIR MIXTURES

A.I. Yakubchik and N.G. Kasatkina

To elucidate the influence of the structure of unsaturated compounds (number and arrangement of the substituents on the carbon atoms with a double bond) on the rate at which ozone adds to them, we constructed the curves for the absorption of ozone by various unsaturated compounds and their mixtures. The curves for the absorption of ozone by mixtures of ethylene compounds with the same substitution character proved to be parallel to the abscissa over nearly the whole extent of the process (for example Fig. 1, Curve 3). These curves are in no way different from the curves for the absorption of ozone by individual compounds with either a double bond or with two isolated double bonds. The curves for the absorption of ozone by mixtures of unsaturated compounds with different degrees of substitution also have the same character (Fig. 1, Curve 2; Fig. 2, Curves 1-4; Fig. 3, Curve 3; Fig. 4, Curve 4*). The last circumstance is evidence that the double bonds of unsaturated compounds, showing different degrees of substitution, are ozonized simultaneously.

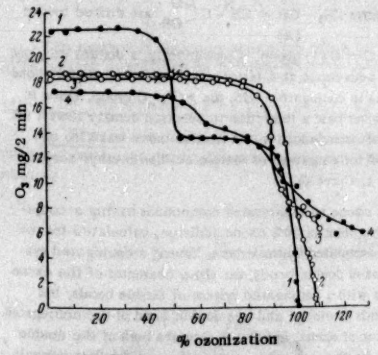


Fig. 1. Ozone absorption curves. 1) Vinylbutylacetylene; 2) mixture of allyl alcohol (49.4%) and methyl-tert-butylethylene (50.6%); 3) mixture of allyl alcohol (45.2%) and styrene (54.8%); 4) mixture of ethyl acrylate (53.1%) and elaidic acid (46.9%).

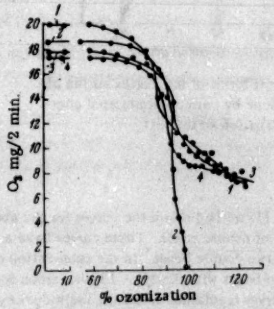


Fig. 2. Ozone absorption curves. 1) Mixture of allyl alcohol (68.3%) and elaidic acid (31.7%); 2) mixture of allyl alcohol (65.5%) and tetramethylethylene (34.5%); 3) mixture of allyl alcohol (50.8%) and elaidic acid (49.2%); 4) mixture of allyl alcohol (33.9%) and elaidic acid (66.1%).

* After saturation of the double bonds the ozone is consumed at a slower rate on either ozonization of the benzene ring or oxidation of the >C = O group.

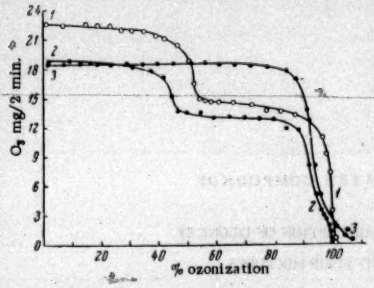


Fig. 3. Ozone absorption curves. 1) Isopropenylacetyl; 2) mixture of diallyl (39.7%) and dimethylacetylene (60.3%); 3) mixture of methyl-tert-butylethylene (46.7%) and tetramethylethylene (53.3%).

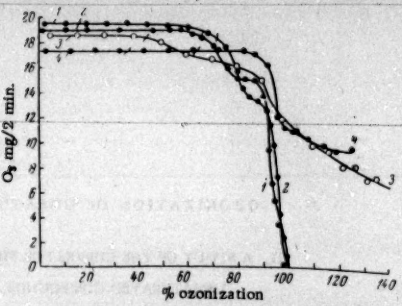


Fig. 4. Ozone absorption curves. 1 and 2) Mixture of diallyl and diisopropenyl; 3) mixture of ethyl cinnamate (58.1%) and elaidic acid (41.9%); 4) mixture of styrene (36.1%) and elaidic acid (63.9%).

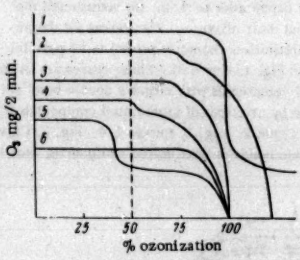


Fig. 5. Typical forms of the curves for the absorption of ozone by various unsaturated compounds. Explanation in the text.

The curve for the absorption of ozone by a mixture of elaidic acid and ethyl cinnamate has a break (Fig. 4, Curve 3). The double bond of the ethyl cinnamate, found in conjugation with the double bond of the >C = O group, adds ozone at a slower rate than does the double bond of elaidic acid, in which molecule the >C = O group is removed from the ethylene bond. In unsaturated compounds, having the >C = O group in conjugation with the ethylene bond, the π-electrons of the latter $CH_2 - CH = CH - C(=O)OR$ (A) are shifted toward the >C = O (A) group. Consequently, a distant ethylene bond adds ozone at a faster rate than does a double bond that is in conjugation with the >C = O group, since in the latter case a reduction in electron density lowers the rate of ozone addition. A similar curve was also obtained for a mixture of elaidic acid with ethyl acrylate (Fig. 1, Curve 4).

Earlier [1] we had shown the curves for the absorption of ozone by unsaturated compounds having a conjugated system of double bonds. These curves have a break at the point of 50% ozone addition, calculated for the saturation of two double bonds. In the ozonization of mixed unsaturated hydrocarbons, having a conjugated system of double bonds with diallyl – a hydrocarbon showing isolated double bonds, the same character of the ozone absorption curves is retained as for the individual hydrocarbons with a conjugated system of double bonds, but here a reduction in the rate begins after both of the double bonds in diallyl and one double bond of the conjugated system have been saturated (Fig. 4, Curves 1 and 2; the percent of ozone, needed to saturate both of the double bonds in diallyl and one double bond in diisopropenyl is shown on the curves by cross marks; on the first curve it is 72%, and 66% on the second).

The absorption of ozone by a double bond and a triple bond, present in either the same or in different molecules, proceeds at a different rate (Fig. 3, Curves 1 and 2; Fig. 1, Curve 1). The slower addition of ozone to the triple bond can be explained by a number of specific characteristics, inherent in the acetylene bond. The triple bond shows electron-acceptor properties. Ozone, possessing great electron affinity, will react with the electron-acceptor triple bond at a slower rate than it does with the double bond. A quantitative account of the fragments in the decomposition products of the ozonide, obtained in the incomplete ozonization of a mixture of diallyl and

dimethylacetylene, supports the sequential order of ozonizing double and triple bonds. The ozonization of a mixture of diallyl with dimethylacetylene was terminated after both of the double bonds in diallyl had been saturated. In the ozonolysis products 90.5% of the carbon skeleton, based on taken diallyl, was accounted for.

Typical forms of the curves for the absorption of ozone by diverse unsaturated compounds are shown in Fig. 5. It follows from an examination of these curves that unsaturated compounds can absorb either a whole number of moles of ozone (Curves 3, 4, 5 and 6) or a fractional number (Curves 1 and 2). Curve 6 fails to show a break. The substance, to which such an ozone absorption curve corresponds, can have either one or several isolated double bonds ([1], p. 1474; Fig. 2, Curve 1 and Fig. 1, Curve 3) or it can have a triple bond ([1], p. 1474; Fig. 1, Curve 4*). The other curves show a break.

Substances, for which the ozone absorption curves are similar to Curve 5 in Fig. 5, can contain both double and triple bonds (Fig. 3, Curves 1 and 2; Fig. 1, Curve 1).** Curve 4 in Fig. 5 is characteristic for compounds, containing either a conjugated system of double bonds ([1], p. 1475; Fig. 4, Curve 1 and Fig. 3, Curve 2) or two double bonds, one of which is found in the ring ([1], p. 1475; Fig. 4, Curve 2). A reduction in the rate occurs at the moment of 50% ozone addition.

Curve 3 in Fig. 5 corresponds to those unsaturated compounds that show several double bonds, of which two are found in conjugation. A reduction in the rate begins not at the moment of 50% ozone addition, but instead considerably later (Fig. 4, Curves 1 and 2). Substances, in the ozonization of which ozone absorption curves are obtained that are similar to Curve 2 in Fig. 5, can contain several double bonds, of which one is found in conjugation with the >C = O group (Fig. 1, Curve 4). Curve 1 in Fig. 5 is characteristic for compounds that contain: a) either double or triple bonds in the benzene ring ([1], p. 1474; Fig. 3, Curve 1 and Fig. 1, Curve 5), and b) double bonds and the >C = O group, not found in conjugation with a double bond ([1], p. 1474; Fig. 1, Curve 2 and Fig. 2, Curve 2). A whole number of moles of ozone are added at the point where the rate drops sharply. The number of double and triple bonds can be calculated from that portion of the curve up to the reduction in rate.

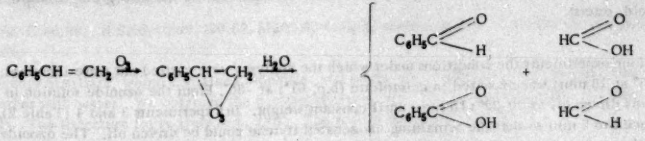
By utilizing the indicated scheme for the separation of the ozone absorption curves it becomes possible to judge from the form of the curve the character of the multiple bonds and their mutual arrangement in an unknown unsaturated compound with a known molecular weight. The number of multiple bonds can be determined from the amount of added ozone.

EXPERIMENTAL

The method of obtaining absorption curves for ozone was described previously [1]. The experimental data of the present work are given in Table 1.

Study of the Products of Ozonolysis at Various Stages of Ozonization

A. Styrene was ozonized four times; during the course of the work, the process of ozone absorption was stopped at various stages in different experiments. Formic acid and formaldehyde were present in the ozonolysis products



* In order to determine what kind of multiple bonds were contained in the investigated substance, it was necessary to plot ozone absorption curves for a mixture of this substance with known ethylene or acetylene compounds. If a continuous curve was obtained in the first case, the investigated substance contained a double bond; if a continuous curve was obtained in the second case, the investigated substance contained a triple bond.

** The number of double bonds may be calculated from the number of moles of ozone absorbed up to the reduction of speed, and the number of triple bonds by the number of moles of ozone absorbed at the lower speed.

TABLE 1

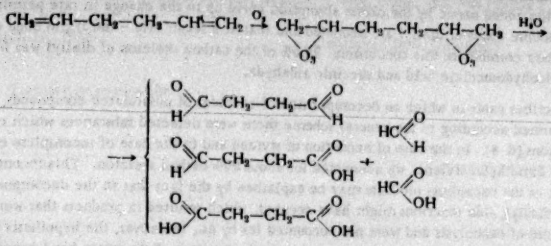
Figure	Curve	Substance	Boiling point	% Ozone: Calculated for components of mixture	% Ozone: Add to mixture
1	1	Vinylbutylacetylene *	63—64° (11 mm)	100.0	99.2
1	2	mixture: allyl alcohol	95—96.5	49.4	107.8
		mixture: methyl-tert-butylethylene	77.5—78	50.6	
1	3	mixture: allyl alcohol	95—96.5	45.2	109.0 **
		mixture: styrene	33—34 (10 mm)	54.8	
1	4	mixture: ethyl acrylate	97—98	53.1	127.7 **
		mixture: elaidic acid	50—51 (m.p.)	46.9	
2	1	mixture: allyl alcohol	95—96.5	68.3	122.0 **
		mixture: elaidic acid	50—51 (m.p.)	31.7	
2	2	mixture: allyl alcohol	95—96.5	65.5	98.5
		mixture: tetramethylethylene	71.5—72	34.5	
2	3	mixture: allyl alcohol	95—96.5	50.8	123.0 **
		mixture: elaidic acid	50—51 (m.p.)	49.2	
2	4	mixture: allyl alcohol	95—96.5	33.9	112.5 **
		mixture: elaidic acid	50—51 (m.p.)	66.1	
3	1	Isopropenylacetylene *	33—34	100.0	101.1
3	2	mixture: diallyl	58—59	39.7	100.0
		mixture: dimethylacetylene	27—28	60.3	
3	3	mixture: methyl-tert-butylethylene	77.5—78	46.7	106.0
		mixture: tetramethylethylene	71.5—72	53.3	
4	1	mixture: diallyl	58—59	43.8	100
		mixture: diisopropenyl	68—69	56.2	
4	2	mixture: diallyl	58—59	32.2	98.8
		mixture: diisopropenyl	68—69	67.8	
4	3	mixture: ethyl cinnamate	270—271	58.1	133.1 **
		mixture: elaidic acid	50—51 (m.p.)	41.9	
4	4	mixture: styrene	33—33.5 (10 mm)	36.1	124.6 **
		mixture: elaidic acid	50—51 (m.p.)	63.9	

* The isopropenylacetylene and vinylbutylacetylene hydrocarbons were obtained by us from A.A. Petrov, and we express our gratitude to him.

** The quantity of ozone exceeding 100% was spent after saturation of the double bonds for the ozonation of the benzene ring (styrene) or for oxidation of the >C = O group (elaidic acid, esters).

In all four experiments the conditions under which the analyses were carried out were identical. Styrene (b.p. 33-33.5° at 10 mm) was ozonated in chloroform (b.p. 61°) at -30°. From the ozonide solution in chloroform the solvent was driven off at 20-22° (15 mm) until constant weight. In Experiments 3 and 4 (Table 2), the pressure was reduced to 2 mm so that the remaining unozonated styrene could be driven off. The ozonide was decomposed with water on heating to the boil in a flask fitted with reflux condenser. Formic acid was quantitatively determined by reduction of mercuric chloride to mercurous [2] in the aqueous solution of the ozonolysis products and formaldehyde was determined by its condensation products with β-naphthol [3]. The results are given in Table 2.

B. A mixture of diallyl and dimethylacetylene was ozonated in ethyl chloride at -70° until decrease in rate, i.e. until addition of ozone to the two double bonds of diallyl:



The solvent was driven off from the ozonide solution at 20° and the unozonated dimethylacetylene at 20° under 150 mm pressure. The ozonide was decomposed with water. Water was driven off from the ozonolysis products at reduced pressure (150 mm at start of experiments and 50 mm towards end) and at a temperature of 60-70°. The ozonolysis products were divided into a viscous liquid and a crystalline portion.

TABLE 2

Exp. No.	Weight of styrene (in g)	Percentage added ozone with respect to percentage calculated on double bond	Weight (in g)		Percentage carbon, determined in formaldehyde and formic acid
			formaldehyde	formic acid	
1	6.22	100.4	0.248	2.099	90.11
2	4.05	100.9	0.049	1.546	90.58
3	7.97	50.6	0.416	0.973	45.65
4	7.03	51.2	0.227	1.102	46.61

The crystalline substance, recrystallized from hot water, had m.p. 182-183°, which corresponded to the melting point of succinic acid. A mixed sample with chemically pure succinic acid gave no melting point depression.

Found %: C 40.45; H 5.38; equiv. 59.32. $C_4H_6O_4$. Calculated %: C 40.66; H 5.13, equiv. 59.02.

The viscous liquid had b.p. 132-135° at 14 mm, which is near the boiling point of aldehydosuccinic acid. (Literature data give b.p. 134-136° at 14 mm [4]).

Found %: C 46.86; H 6.56; equiv. 100.87; M 103.0. $C_4H_6O_5$. Calculated %: C 47.03; H 5.92; equiv. 102.05. M 102.05.

The aqueous distillate, which contained aldehydes and acids, was neutralized and the aldehydes were distilled off together with water. We obtained the p-nitrophenylhydrazone of succinic aldehyde [5]. M.p. 177-178° (from alcohol). The literature for it gives m.p. 178°. The results are given in Table 3.

TABLE 3

Diallyl	Weight (in g)			Carbon content (in %)		
	Succinic acid	Aldehydo-succinic acid	Succinic aldehyde	Succinic acid	Aldehydo-succinic acid	Succinic aldehyde
5.92	2.05	4.02	0.73	24.00	54.62	11.85

A total of 90.5% carbon skeleton was accounted for in the ozonolysis products, which contained 4 carbon atoms. Examination of the added ozone by the ozone absorption curve up to the change in rate permits us to conclude that at first both double bonds of diallyl are ozonated and that at a lesser rate – the triple bond of dimethylacetylene. Analytical data corroborate this conclusion: 90.5% of the carbon skeleton of diallyl was found in the form of succinic acid, aldehydosuccinic acid and succinic aldehyde.

The literature describes cases in which on decomposition of ozonides of unsaturated compounds, together with the products that formed according to the general scheme there were detected substances which could have resulted from side reactions [6-8]. In the case of ozonation of styrene and in the case of incomplete ozonation of a mixture of diallyl and dimethylacetylene, we accounted for about 90% carbon skeleton. This incomplete account of carbon skeleton in the ozonolysis products may be explained by the fact that in the decomposition of the ozonides of styrene and diallyl, side reactions might have occured, which resulted in products that were not foreseen in the general scheme of ozonolysis and were not accounted for by us. Moreover, the hypothesis is plausible that in the reaction zone, at a more rapid rate, there occurs a partial ozonation of the triple bond concurrently with the double bond, as in the reaction zone, at a lesser rate, there occurs a partial ozonation of the double bond concurrently with ozonation of the triple bond. It is possible that during the ozonation of styrene there occurs partial ozonation of the benzene ring, simultaneously with ozonation of the double bond, in the same manner as, simultaneously with the aromatic ring, there occurs partial ozonation (about 10%) of the double bond.

The method of obtaining ozone absorption curves which we devised was used by A.I. Lebedeva, T.A. Mishnina and R.P. Ryskina for the ozonation of certain acetylenic compounds [9].

SUMMARY

1. Unsaturated compounds can add either a whole or a fractional number of moles of ozone. A fractional number of moles of ozone is absorbed by compounds that contain a >C = O group, the tert-butyl radical and the benzene ring.

2. Compounds that absorb a whole number of moles of ozone correspond to the ozone absorption curves: 1) without a break (compounds having either one or several isolated double bonds, and acetylene compounds), and 2) with a break (compounds that contain: a) double and triple bonds, b) a conjugated system of double bonds, c) several double bonds, of which two are found in conjugation, and d) two double bonds, one of which is found in the ring).

3. For unsaturated compounds, showing the absorption of a fractional number of moles of ozone, curves were obtained with a break, characteristic for substances that contain: a) double bonds and the benzene ring, b) triple bonds and the benzene ring, and c) several double bonds, of which one is found in conjugation with the >C = O group.

4. From the form of the ozone absorption curves it is possible to judge as to the character of the multiple bonds and their mutual arrangement. The amount of ozone at different portions of the curve can be calculated and the number of bonds and which bonds are ozonized first and at the fastest rate can be determined.

5. The possibility of determining the structure of the substance being ozonized from the shape of the ozone absorption curve was confirmed by analyzing the ozonolysis products of styrene and a mixture of diallyl with dimethylacetylene.

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Leningrad State University

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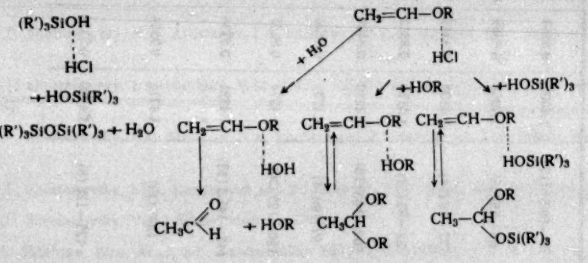
OXYGEN-CONTAINING ORGANOSILICON COMPOUNDS

V. PREPARATION OF ORGANOSILICON COMPOUNDS

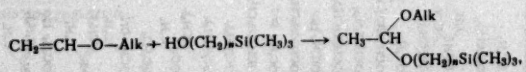
M.F. Shostakovsky, I.A. Shikhiev and V.I. Belyaev

In previous communications [1-5] it was shown that the simple vinyl ethers of primary, secondary and tertiary alcohols easily react with alkyl(aryl)silanols in the presence of small amounts of hydrochloric acid. In this work it was established that here two concurrent reactions proceed simultaneously – both acetalization and dehydration of the silanols. The latter reaction is especially characteristic for the lower members of trialkylsilanols (trimethyl-, dimethylethyl- and methyldiethylsilanols), which in the presence of 0.1 ml of hydrochloric acid (for 0.2-0.4 mole of starting products) form instead of the organosilicon acetal the corresponding disiloxane, symmetrical alkyl acetal and acetaldehyde.

Only the use of trace amounts of hydrochloric acid (0.003 g for 0.2-0.4 mole of starting products) leads to the formation of the organosilicon acetal. In general form the formation of organosilicon acetals from simple vinyl ethers and silanols, from the viewpoint of the oxonium theory, developed by one of us [6], can be shown by the scheme:

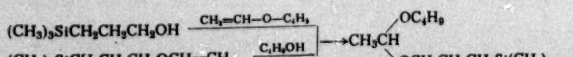


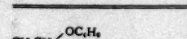
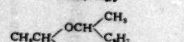
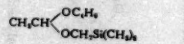
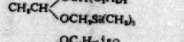
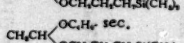
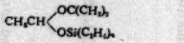
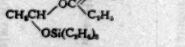
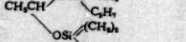
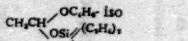
In this work it was also shown that the acetalization reaction for trimethylsilylmethanol and trimethylsilyl-γ-propanol proceeds with excellent yield under conditions analogous to those used in the case of organic alcohols [6], in accord with the scheme:



where n = 1 and 3.

Together with this, one of us had also studied earlier [7] the previously unknown reaction of simple vinyl ethers with a γ-organosilicon alcohol, where the structure of the butyltrimethylsilylpropyl acetal was proved in two ways:



Formula	Boiling point at pressure (in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calculated	Found % C	Found % H	Found % Si	Calculated % C	Calculated % H	Calculated % Si	Yield (in %)
	56—56.5° (17)	1.4006	0.8264	55.90	55.96	56.46, 56.39	11.83, 11.74	14.42, 14.79	56.84	11.57	14.73	56.8
	64—65 (13)	1.4068	0.8369	60.07	60.59	59.64, 59.40	11.81, 11.78	13.28, 13.37	58.78	11.84	13.73	35.3
	77—78 (14)	1.4130	0.8342	61.04	61.60	59.49, 59.70	11.66, 11.89	12.91, 12.86	58.78	11.84	13.74	69.0
	82—83 (12)	1.4116	0.8312	65.29	66.23	60.55, 60.45	11.83, 11.85	13.46, 13.65	60.50	12.01	12.94	62.0
	102—103 (13)	1.4240	0.8409	70.56	70.86	62.20, 62.40	12.10, 12.23	11.53, 11.80	62.01	12.13	12.07	59.6
	97—98 (6)	1.4249	0.8424	70.53	70.86	62.47, 62.29	11.98, 11.94	12.09, 12.24	62.01	12.13	12.07	57.4
	120—123 (30)	1.4274	0.8631	69.37	69.85	62.49, 62.60	12.20, 12.25	11.74, 11.88	62.01	12.13	12.07	55.7
	145—145.5 (53)	1.4331	0.8735	73.33	74.48	63.26, 63.58	12.09, 11.93	11.42, 11.49	63.36	12.27	11.39	53.5
	139° (19)	1.4715	0.9314	79.90	80.26	68.05, 67.96	9.64, 9.53	11.08, 11.86	67.62	9.84	10.53	62.3
	125—126 (8)	1.4770	0.9356	84.56	84.89	68.79, 68.71	9.97, 9.97	10.14, 9.98	68.52	10.06	10.00	58.5

The synthesis of the indicated mixed organosilicon acetal at the same time also demonstrates the structure of this class of acetals.

EXPERIMENTAL

1. Butyltrimethylsilyl acetal. In an ampul (cooled to -10°*) was placed 10 g (0.2 mole) vinylbutyl ether (b.p. 92-93°, n_D^{20} 1.4026, d_4^{20} 0.7793), 18 g (0.2 mole) trimethylsilanol (b.p. 98-98.6° at 757 mm, n_D^{20} 1.3892, d_4^{20} 0.8139) and to this was added about 0.003 g 33% hydrochloric acid. The sealed ampul was heated in a thermostat at 65-67° for 12 hours; it was then opened and its contents were dried with potash and vacuum-distilled. Fractions were separated at 17 mm: 1st 52-55°, 4.2 g (n_D^{20} 1.3992), 2nd 56-56.5°, 21.6 g.

The substance with b.p. 56-56.5° at 17 mm was butyltrimethylsilyl acetal. Yield 56.84%, based on taken vinylbutyl ether; the constants and analytical data for the substance are given in the table.

To sum up the investigation that was carried out on the reaction of vinyl ethers with triethyl-, dimethylphenyl- and diethylphenylsilanols and α- and γ-organosilicon alcohols in the presence of 0.1 ml hydrochloric acid, the corresponding organosilicon acetals were obtained, the characteristics of which are given in the table.

SUMMARY

1. It was established that two concurrent reactions proceed simultaneously in the reaction of simple vinyl ethers with silanols – acetalization and dehydration of the silanols.

2. Based on the oxonium theory a scheme was proposed for the formation of acetals from simple vinyl ethers and silanols.

3. Ten new mixed organosilicon acetals were synthesized and described.

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Institute of Organic Chemistry of Academy of Sciences USSR

* Cooling to -10° is necessary to prevent the dehydration reaction of trimethylsilanol.

** T.p. = C.B. Translation pagination.

CATALYTIC AMINATION OF ORGANIC COMPOUNDS

III. THE CATALYTIC AMINATION OF ETHERS AND ESTERS OF PHENOL

N.S. Kozlov and L.F. Akhmetshina

In our previous communication [1] we had studied the catalytic amination of phenols with compressed ammonia. Here it was established that the introduction of compressed ammonia into the reaction strongly facilitates the conversion of phenols into aromatic amines.

To develop this direction we investigated in the present study the catalytic amination of the ethers and esters of phenol with compressed ammonia. This type of study had not been made before. The phenol ethers and esters subjected to amination were: anisole, phenetole, phenyl butyl ether, diphenyl ether, and finally, phenyl acetate. It was revealed that the amination of the phenol ethers and esters proceeds only if the reaction is run at 450-575° in the presence of aluminum oxide and with the introduction of ammonia, compressed to 8-9 atmospheres. Under these conditions we obtained aniline, p-toluidine and p-cresol from anisole; and aniline, o-ethylaniline, o-ethylphenol and ethylamines from phenetole. From butyl phenyl ether we obtained aniline and butylene. The only amination product isolated from the diphenyl ether proved to be aniline.

From the literature [2-5] it is known that the passage of the vapors of phenol ethers over oxide catalysts heated to 400° results in their pyrolysis with the formation of aromatic hydrocarbons. In our experiments it was shown that the pyrolysis of phenol ethers fails to proceed in a compressed ammonia atmosphere at elevated temperatures. Only cleavage of the phenol ethers by the ammonia proceeds under these conditions, a fact that has not been mentioned before in the literature.

The formation of aromatic amines from ammonia and phenol ethers can be depicted by Equations (1) and (2), which were proposed earlier [6] for the ammonolysis of straight ethers. The formation of alkylated phenols and fatty-aromatic amines in these reactions is most probably explained by, first, the isomeric transformation of the phenol ethers into alkylated phenols with subsequent amination of the isomerization product and, second, as the result of the isomeric transformation of the fatty-aromatic amines into primary aromatic alkylamines. This type of representation is supported by literature data [7,8].

The reaction of phenyl acetate with ammonia was studied earlier by Sabatier [9], who, on passing vapors of phenyl acetate with ammonia over catalysts (either aluminum oxide or thorium oxide) heated to 480-490°, obtained phenol and acetonitrile. Consequently, in that reaction, only one part of the phenyl acetate suffered amination. Under our studied conditions we obtained aniline and acetonitrile from phenyl acetate and compressed ammonia. We were the first to realize this transformation of phenyl acetate into aniline and acetonitrile.

EXPERIMENTAL

The experiments involving catalytic amination of phenol ethers and esters were carried out as follows. A weighed portion of the ether (ester) in the ammonium stream was passed at a fixed rate over the heated catalyst (pressed active aluminum oxide). The experiments were carried out in the previously described apparatus [10]. The dependence was studied of the yield of reaction products on the temperature, ammonia pressure and rate of introduction on the substance on the catalyst. It was found that when ammonia was introduced into the reaction under ordinary pressure and the reaction was carried out at a temperature below 400°, there was no formation of aromatic amines. The greatest yield of aromatic amines was obtained in the case when the reaction was carried out at 450-475°, when the ether (ester) was introduced at the rate of 6-10 drops per minute and when compressed (to 8-9 atm.) ammonia was introduced into the reaction. The catalyzate was treated in accordance with the

usual methods, the amines were isolated through salts of hydrochloric acid and the phenols were extracted with alkali. The individual amines, phenols and neutral products that were obtained were distilled and analyzed. The phenols were analyzed according to S.S. Nametkin's method [11] and the amines were characterized in the form of crystalline derivatives of phthalic anhydride.

1st experiment. From the catalyzate, obtained after amination of 23 g anisol, was obtained 0.5 g anisol, 7 g phenols and 12 g amines. From the phenol fraction was isolated phenol and p-cresol. Distillation of the amines yielded the following fractions: 1st fraction, b.p. 180-190°, 5.0 g; 2nd fraction, b.p. 190-205°, 4.0 g; 3rd fraction, 205-245°, 1.5 g; residue 1 g. From these fractions were isolated aniline and p-toluidine, which were characterized by the crystalline derivatives of phthalic anhydride. The yield of amines was 52.68% on the anisole taken for reaction.

2nd experiment. From the catalyzate, obtained after amination of 23 g phenol, was isolated 0.5 g phenetole, 7 g phenols and 10.4 g amines. The phenols distilled in the range 180-220°; from them was isolated phenol and o-ethylphenol (b.p. 205-208°, d_4^{20} 1.0241; the o-ethylphenylhydroxyacetic acid, prepared from it, had m.p. 140-141°; literature data give m.p. 141°). The amines were initially heated in a Wurtz flask on a water bath and the volatile products were absorbed in a hydrochloric acid washer. Analysis of the obtained hydrochloride by the K.G. Mizuch-A.Ya. Savchenko [12] method revealed the presence of ethylamine and diethylamine. The remaining amines distilled in the range 180-220°; from this fraction was isolated aniline and o-ethylaniline (b.p. 215-217°, d_4^{20} 0.9871; the benzene derivative had m.p. 146-147°; literature data give m.p. 147°). The yield of amines was 45.6% on the phenetole taken.

3rd experiment. Amination of 22 g butyl phenyl ether yielded 5.5 liter gas of an unsaturated character, which we took to be all butylene. 9.1 g amines was obtained; no aliphatic amines were found among these. Distillation yielded the following amine fractions: 1st fraction had b.p. 180-190°, 6.5 g; 2nd fraction had b.p. 190-220°, 2.0 g. The first fraction consisted mainly of aniline. No butylaniline derivatives could be isolated. Evidently, both butylamines and butylanilines were unstable under the conditions of our experiment. Yield of amines was 66.7% on butyl phenyl ether taken for reaction.

4th experiment. Of all the phenol ethers which we studied, diphenyl ether proved the most stable. Thus, on amination of 18 g diphenyl ether, from the catalyzate was isolated 13.3 g initial product and 3.6 g aniline. The yield of aniline was 18.3% on taken or 70% on reacted diphenyl ether.

5th experiment. After amination of 23 g phenylacetate, from the catalyzate was isolated: 1.5 g initial product, 2 g acetonitrile (b.p. 79-83°, d_4^{20} 0.7917, n_D^{20} 1.346) and 14.7 g aniline. The yield of acetonitrile was 28.9% and of aniline 92.24%, on phenyl acetate taken for reaction. We believe that the low yield of acetonitrile was due to the fact that at the high temperature of the experiment, acetonitrile decomposed.

SUMMARY

1. We were the first to study the catalytic amination of phenol ethers with compressed ammonia. As the result of ammonolysis the phenol ethers are converted into aromatic amines with small amounts of aliphatic amines as impurities.

2. The catalytic amination of phenyl acetate with compressed ammonia gave aniline and acetonitrile.

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ACTION OF NITROGEN PEROXIDE ON UNDECYLENIC ACID

S.V. Vasilyev

In connection with the fact that the double bond in undecylenic acid is considerably removed from the carboxyl group, and also in connection with the presence of a $CH_2 = CH -$ group in the molecule, it seemed of interest to determine how undecylenic acid would behave toward nitrogen peroxide ($2NO_2$).

N.Ya. Demyanov [1] established that hydrocarbons of the ethylene series, containing the $CH_2 = CH -$ group, under treatment with nitrogen peroxide and subsequent reduction give diamines. If the rule established by N.Ya. Demyanov is also observed with respect to unsaturated acids, then undecylenic acid, under treatment with nitrogen peroxide and subsequent reduction, should give the corresponding diamino acid.

Undecylenic acid was treated in dry ether solution at 0° with both gaseous and liquid nitrogen peroxide.

Treatment of the undecylenic acid in ether solution with gaseous nitrogen peroxide gave a liquid addition product. The substance decomposed on storage, evolving nitrogen oxides; here a crystalline substance deposited in the precipitate.

On the basis of study and analytical data the crystalline substance was assumed to be nitrohydroxyundecylenic acid. As regards the original liquid addition product –, on the basis of its instability, behavior toward water and toward alcoholic alkali solution (the liberation of either nitrous acid or its salts), and also judging by the fact that nitrohydroxyundecylenic acid is obtained from it, this product can be characterized as being the nitrite ester of nitrohydroxyundecylenic acid.

Treatment of undecylenic acid with liquid nitrogen peroxide under the same conditions gave analogous results. Thus, the gradual addition of the reagent to a solution of 75.0 g of the acid in 130 ml of ether gave 108.5 g of yellow oily addition product. The substance showed the properties described for the addition product obtained with gaseous nitrogen peroxide; it was soluble in ether, alcohol and acetone; when shaken with water it evolved nitrous acid. When allowed to stand in the air the product decomposed with the liberation of nitrogen oxides; here the crystalline nitrohydroxyundecylenic acid (m.p. 121.5-122°) was deposited. The acetyl derivative of the acid melted at 85-87°.

Both the original addition product and the nitrohydroxyundecylenic acid, either under prolonged heating with water or when oxidized with potassium permanganate, are decomposed at the location of the previously existing double bond in the original acid with the formation of an acid having a lower number of carbon atoms.

The reduction of the nitrohydroxyundecylenic acid with tin and hydrochloric acid gave a small amount of the hydrochloride of aminohydroxyundecylenic acid. Here the main reaction product was sebacic acid and hydroxylamine hydrochloride. The use of other reduction methods (tin and hydrochloric acid in alcohol medium, iron filings in acetic acid solution, metallic sodium in anhydrous alcohol, ammoniacal ferrous sulfate solution) failed to give positive results.

Consequently, the treatment of undecylenic acid with either gaseous or liquid nitrogen peroxide gave the nitrosite, which then underwent transition into the nitrohydroxyundecylenic acid:

$$\underset{\text{ONO}\quad\text{NO}_2}{\text{CH}_2\text{CH}(\text{CH}_2)_8\text{COOH}} \rightarrow \underset{\text{HO}\quad\text{NO}_2}{\text{CH}_2\text{CH}(\text{CH}_2)_8\text{COOH}}.$$

The secondary nature of the nitro group in the nitrohydroxyundecylenic acid was shown by its reactions with potassium nitrite and sulfuric acid and by the M.I. Konovalov method [2].

Both the observations made during our work and the experimental results revealed that moisture plays an essential role in the formation of the crystalline nitrohydroxyundecylenic acid, but here the amount of water should be very small.

As a result, when the results of the studies made by N.Ya. Demyanov and K.V. Sidorenko [3,4] on ethylene hydrocarbons are compared with ours [5,6], a relationship is found to exist between the behavior of the starting substances toward nitrogen peroxide and their structure. In our case the nitrogen peroxide adds to undecylenic acid in such a manner that the ONO (or OH) group adds to the most hydrogenated carbon atom, and the NO_2 group – to the least hydrogenated.

EXPERIMENTAL

Addition of nitrogen peroxide to undecylenic acid. A solution of 73.0 g undecylenic acid in 125 ml dry ether was saturated with nitrogen peroxide at 0°. As the gas was passed in, the solution colored yellow, which became green and then went to brown. When saturation of the double bond of the acid was complete, the solution was filtered and on cooling, the solvent was removed by a stream of carbon dioxide. 103.0 g amber-colored oily addition product was obtained with an iodine number of 0. To remove the excess of nitrogen peroxide and other admixtures, the substance was transferred to a separating funnel and was shaken 3 times with new portions of dry low-boiling petroleum ether.

The analysis for nitrogen gave a result (7.96, 8.17%), which corresponded to a mixture of mononitro ($C_{11}H_{21}NO_5$) and dinitro ($C_{11}H_{20}N_2O_8$) derivatives. The addition product was soluble in ether, ethyl acetate, alcohol, acetone; it was insoluble in water, petroleum ether, ligroine. On shaking with water, nitrous acid separated out and upon shaking with alcoholic caustic potash solution, the nitrite came down.

When the addition product was heated with acetic anhydride, the acetyl derivate was obtained; strong resinification took place. From 5.0 g of substance taken for reaction, 0.4 g of crystalline product was obtained with m.p. 84.5-87°. Analysis of the acetyl derivative gave the following result.

Found %: C 53.86, 53.90; H 8.16, 7.94; N 4.95, 4.31. $C_{13}H_{23}NO_5$. Calculated %: C 53.98; H 7.96; N 4.84.

On standing the addition product was decomposed, gave off nitrogen oxides and crystals came down. After 5-6 days under a glass bell jar, the liquid substance had completely crystallized. When kept without access of moisture, the substance did not crystallize for a long time.

The crystalline compound was in the form of light-yellow flakes, soluble in ether, ethyl acetate, methyl, ethyl, propyl, butyl, amyl alcohols, acetone, carbon tetrachloride; it was insoluble in water, petroleum ether. M.p. 121-122° (from alcohol). The analytical results corresponded to nitrohydroxyundecylenic acid.

Found %: C 53.75, 53.58; H 8.40, 8.06; N 5.62, 5.55. $C_{11}H_{21}NO_5$. Calculated %: C 53.44; H 8.5; N 5.67.

Heating of the addition product with water. 10.0 g of freshly prepared product of the reaction of nitrogen peroxide with undecylenic acid was heated for 30 hours with 100 ml water in a flask fitted with reflux condenser on a water bath. The aqueous layer colored yellow and contained nitrous acid. On cooling the solution, a colorless precipitate (6.6 g) came down. The crystalline substance was soluble in ether, alcohol, ethyl acetate, benzene and chloroform. After recrystallization from alcohol, the substance melted at 129-130°. A mixed sample with sebacic acid gave no depression. The analytical results also corresponded to sebacic acid (C 59.76, 59.48%; H 8.54, 8.71%). Similar results were obtained upon oxidation of the addition product with potassium permanganate in alkaline as well as in neutral medium.

Reduction of nitrohydroxyundecylenic acid. 200.0 g tin was placed in a flask fitted with reflux condenser, thermometer and dropping funnel. Hydrochloric acid and nitrohydroxyundecylenic acid was introduced in small portions. On adding the calculated amount of hydrochloric acid and 33.0 g substance, the reaction mixture was heated on a water bath. The reaction liquid was filtered off, the filtrate was cooled and the precipitate was separated off; the yield was 23.2 g sebacic acid, m.p. 130-130.5° (C 59.33, 59.68%; H 8.31, 8.18%). The filtrate from the sebacic acid was treated with hydrogen sulfide, lead oxide and was then steamed to dryness. The residue was extracted with anhydrous alcohol. The alcoholic extract was cooled; we isolated 3.6 g hydroxylamine hydrochloride (m.p. 151-158.5°, with decomp.).

On removal of the alcohol, 0.74 g substance was isolated which contained nitrogen and chlorine. The colorless hygroscopic compound was soluble in water and alcohol; it was insoluble in ether. The prepared compound melted at 193-194.5° (with decomp.).

Found %: C 45.61, 45.49; H 9.57, 9.77; N 4.68, 4.64; Cl 12.12, 12.05. $C_{11}H_{23}NO_3 \cdot HCl \cdot 2H_2O$. Calculated %: C 45.59; H 9.67; N 4.84; Cl 12.26.

The experimental data and the analytical results permit characterization of the obtained compound as the hydrochloride of aminohydroxyundecylenic acid.

SUMMARY

1. It was established that the double bond in undecylenic acid is completely saturated by both gaseous and liquid nitrogen peroxide with the addition of both ONO and NO_2 groups; here the nitro group adds to the least hydrogenated carbon atom, and the ONO group to the most hydrogenated.

2. The reaction of nitrogen peroxide with undecylenic acid differs from its reaction with ethylene hydrocarbons containing the $CH_2 = CH -$ group, the latter giving dinitro compounds.

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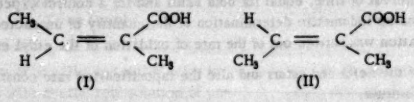
THE CONFIGURATION AND PROPERTIES OF UNSATURATED ACIDS AND THEIR DERIVATIVES

V. THE PROPERTIES OF ANGELIC AND TIGLIC ACIDS AND THEIR ESTERS

A.K. Plisov and A.P. Kostyuk

Angelic and tiglic acids enter into the composition of many natural medicinal plants and are a component part of a number of medicinal preparations. Tiglic acid was recently isolated from the decomposition products of sodium penicillin. Angelic acid is found in the free state in the roots of the angelica plant (Angelica archangelica), and as the amyl and other esters in the oil of the Roman camomile, in which tiglic acid is also present. The triglyceride of tiglic acid is found in croton oil. It was established quite recently that the favorable influence exerted by digitalis on the cardiac-vascular system is conditioned to a large degree by the presence in it of angelic acid as the lactone. The derivatives of angelic acid find use in the manufacture of plastics, and serve as material for the preparation of coatings for articles made from protein plastics and other products.

Nevertheless, the question as to the configuration of angelic and tiglic acids still remains unanswered, since at the present time there do not exist reliable experimental data on which a decision as to whether these acids belong to either the cis or trans series can be based. Tiglic and angelic acids are considered to be cis-trans isomers, having the configurations corresponding to (I) and (II):



(I) (II)

Two opinions exist as to which of these configurations belong to angelic acid, and which to tiglic acid [1]. Angelic acid, being the low-melting isomer, is most frequently assigned the cis configuration, and tiglic acid the trans configuration. But there also exists a contrary opinion [2].

One of us [3] has already illuminated the problem of the geometric isomerism and reactivity of a number of unsaturated acids. Here it was established that the chemical activity of the acids is found to be in full accord with the steric hindrance theory. To a large degree the question as to the actual configuration of tiglic and angelic acids can be illuminated chemically, if it is considered in this case, as for the other acids already studied by us, that here the radicals at the double bond should exert an analagous influence on their chemical activity.

From the viewpoint of the steric hindrance theory the structure of angelic and tiglic acids should show an influence on their properties: such reactions at the double bond as halogenation, hydrogenation, addition of hydrogen halide acids, oxidation, etc. should proceed with more difficulty for Form (II) than for Form (I), since the space around the double bond in Form (II) is filled, on one side, by two methyl radicals, and on the other side, by hydrogen and the large carboxyl radical. For Form (I) the space near the double bond is filled, on one side, by the methyl and carboxyl radicals, and on the other side, by hydrogen and the methyl radical.

The carboxyl radical fills the space near the double bond to a higher degree than does the methyl radical. This is supported by the values for the volumes of these substituents, calculated at the boiling point by the Kopp formula. The volumes are: for $-CH_3$ 27.6, and for $-COOH$ 36.5 cm^3/mole.

As regards the chemical influence of the radicals, then here, apparently, it can be assumed to be the same for both forms.

We used an acetic acid solution of potassium bichromate to study the oxidation of the acids and of their ethyl esters. It was established that angelic acid and its ethyl ester show more rapid oxidation than do tiglic acid and its ester. As regards the saponification of the esters of these acids, then logically a lower activity should be assumed for the cis form since in this case access of the alkali elements to the ester group will be hindered by the presence of the methyl group at the β-carbon of the double bond; for the trans form this methyl group in its spatial position will not hinder reaction at the ester group, and consequently the saponification of esters, having the trans configuration, should proceed with greater ease than in the first case.

The results of our saponification experiments revealed that the ethyl ester of angelic acid is saponified at a slower rate than is the ethyl ester of tiglic acid. On the basis of these experiments it is necessary to assign the cis configuration (I) to angelic acid, and the trans configuration (II) to tiglic acid.

EXPERIMENTAL

Synthesis of angelic and tiglic acids. Angelic and tiglic acids were synthesized starting from primary butyl alcohol via α-hydroxymethylethylacetic acid. Upon dehydration, the latter was converted to a mixture of angelic and tiglic acids, which was separated by fractional distillation in vacuum. The obtained acids had the following constants: angelic acid: m.p. 45-46°, b.p. 88-90° (12 mm); tiglic acid: m.p. 64°, b.p. 95-96° (12 mm).

Ethyl tiglate was prepared by the method of esterification in a Soxhlet apparatus using CaC_2 to collect the water of reaction. Ethyl tiglate was a colorless liquid with a faint odor. It was readily soluble in alcohol, ether and benzene. B.p. 152-154°.

Ethyl angelate was prepared from the potassium salt of angelic acid and ethyl bromide on heating to 75-80°; it was quite readily soluble in alcohol, ether and benzene. B.p. 140-142°.

The rate of oxidation of the acids and their esters was observed by iodometric determination of the quantity of unreacted oxidant. The experiments were carried out at 25° in small flasks with ground stoppers. 0.01 N solutions of the acids were prepared in the corresponding solvents (benzene, toluene, ether) and were placed in a thermostat. In the same thermostat were placed solutions of potassium bichromate in glacial acetic acid. After the solutions were at the temperature of the thermostat, a suitable amount (3 ml) of solution of the acid being investigated was taken in a micropipet and poured into the small flask with an acetic acid solution of $K_2Cr_2O_7$ (52 ml). After a definite interval of time, equal for both acids and for a control experiment, 5 ml samples were taken with the pipet and an iodometric determination of the quantity of unreacted oxidant was carried out. An analogous determination was carried out of the rate of oxidation of the ethyl esters of the acids.

The oxidation rate constants of the acids and esters and also the saponification rate constants of the esters were in all cases calculated by the formula:

$$K = \frac{1}{t\,(a-b)} \cdot \log \frac{b\,(a-x)}{a\,(b-x)} .$$

Table 1 and Figs. 1-3 give the results of the oxidation experiments we carried out for angelic and tiglic acids.

When a bichromate solution, twice as concentrated, was used for the oxidation, the rate of the reaction increased somewhat, but the ratio of the activities of the cis and trans forms remained the same as before.

Saponification of ethyl angelate and ethyl tiglate. Weighed portions of ester (0.0214 g each) were dissolved in 0.5 ml alcohol and mixed with 20 ml alcoholic KOH. The initial concentration of KOH was 0.00288 N; of saponified ester – 0.1321 N. The remaining alkali was determined acidimetrically.

The experimental data indicate that the spatial configuration of stereo-isomers of angelic and tiglic acids has a marked effect on their rate of oxidation at the double bond. Angelic acid and its ester are more rapidly oxidized than tiglic acid and its ester, which indicates that the double bond of angelic acid is more accessible to the action of the oxidizing reagent than the double bond of tiglic acid. The solvent somewhat changes the relative rate of oxidation of the acids, but in all cases studied angelic acid was oxidized more rapidly than tiglic acid.

The results of the saponification experiments clearly show that this reaction goes more slowly in the case of ethyl angelate.

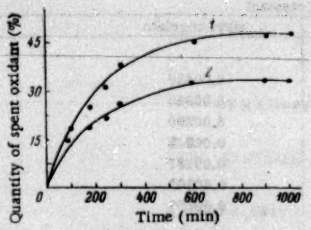


Fig. 1. Oxidation of angelic and tiglic acids in benzene solution with acetic acid solution of potassium bichromate at 25°; 1) angelic acid; 2) tiglic acid.

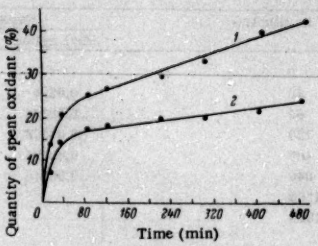


Fig. 2. Oxidation of angelic and tiglic acids in toluene solution with acetic acid solution of potassium bichromate at 25°; 1) angelic acid; 2) tiglic acid.

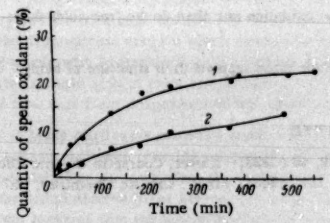


Fig. 3. Oxidation of angelic and tiglic acids in ethereal solution with acetic acid solution of potassium bichromate at 25°; 1) angelic acid; 2) tiglic acid.

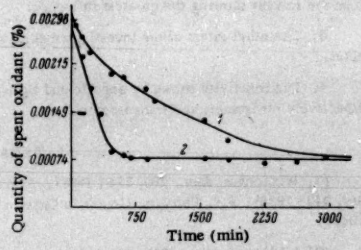


Fig. 4. Hydrolysis of ethyl esters of angelic and tiglic acids with alcoholic KOH solution at 25°; 1) ethyl angelate; 2) ethyl tiglate.

TABLE 1

Oxidation of Angelic and Tiglic Acids with Acetic Acid Solution of Potassium Bichromate at 25°

Solvent of investigated acid	Concentration of acetic acid solution of $K_2Cr_2O_7$	Mean value of oxidation rate constant	
		tiglic acid	angelic acid
Benzene	0.00228 N.	0.0118	0.0607
Toluene	0.00249 N.	0.0657	0.08819
Ether	0.00239 N.	0.01917	0.04971

TABLE 2

Saponification of Ethyl Angelate and Ethyl Tiglate with Alcoholic Caustic Potash Solution at 25°

Time (in minutes)	Saponification rate constant	
	ethyl tiglate	ethyl angelate
0	–	–
30	0.0224	0.00450
60	0.00834	0.00340
120	0.00573	0.00290
480	0.00594	0.00202
840	0.00445	0.00161
1560	–	0.00165
1920	–	0.00157

SUMMARY

1. It was established that tiglic and angelic acids and their ethyl esters manifest different reactivity; angelic acid and its ethyl ester are oxidized more rapidly than are tiglic acid and its ester.

2. The solvent exerts an influence on the oxidation rate of both angelic and tiglic acids; ether proves to be the solvent showing the greatest influence.

3. The ethyl esters of the investigated acids show a slower oxidation rate than do the free acids themselves.

4. The reactivity shown by angelic and tiglic acids and their esters supports their structure as being respectively cis isomers and trans isomers.

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SYNTHESES WITH ACRYLONITRILE

XXVI. SYNTHESIS OF SOME β-ALKOXYPROPIONAMIDES

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The cyanoethylation of alcohols gives β-alkoxy nitriles in good yields, which can then be saponified to the corresponding acids [1]. The saponification of these compounds to the amides has not been studied. The anomalous behavior shown by this type of nitriles is indicated in the literature, and specifically, both in acid [2] and in alkaline medium [3], cleavage of the alkoxy group was observed.

As our basic study subject we chose β-butoxypropionitrile, which is easily obtained by the reaction of acrylonitrile with butyl alcohol [4]. It was found that heating of this substance with aqueous alkali gives β-butoxypropionic acid (in which connection partial cleavage of butyl alcohol is also observed). Heating of the nitrile with hydrochloric acid also gave β-butoxypropionic acid in 63% yield. Saponification with concentrated sulfuric acid at room temperature gave the amide in about 20% yield; however, it was difficult to purify the substance from ammonium sulfate, since the amide is quite soluble in water.

Many nitriles are smoothly converted into amides by the Radziszewski method [5], i.e., under the influence of aqueous hydrogen peroxide solution in weakly alkaline medium. Usually a 3% hydrogen peroxide solution is used; however, in some cases the concentration is raised to 6 and even to 30% [6]. Good results are obtained if either ethyl alcohol [6] or acetone [7] are added to the reaction mixture. We ran a series of experiments, where it was revealed that the saponification of β-butoxypropionitrile proceeds smoothly with 3% hydrogen peroxide solution. An increase in the peroxide concentration to 6% leads to the formation of only β-butoxypropionic acid, in which connection a part of the nitrile is recovered unchanged. The reaction fails to go in neutral medium; the best results are obtained if 0.2-0.3% sodium hydroxide solution is used and alcohol is added until the mixture is homogeneous.

In view of the possibility of over-cyanoethylation (in alkaline medium) we ran the counter synthesis of this amide via the acid and acid chloride:

$$C_4H_9OH + CH_2=CHCN \rightarrow C_4H_9OCH_2CH_2CN \rightarrow C_4H_9OCH_2CH_2CONH_2$$

$$C_4H_9OCH_2CH_2COOH \rightarrow C_4H_9OCH_2CH_2COCl \rightarrow C_4H_9OCH_2CH_2CONH_2$$

The saponification conditions selected in this manner were used to prepare other β-alkoxy amides, in which connection good yields were obtained in all cases. β-Methoxy-, β-ethoxy- [3] and β-butoxypropionitriles, and also the β-cyanoethyl ether of β-butoxyethanol, gave amides in practically quantitative yields. β,β'-Dicyanodiethyl ether [3] and the β,β'-dicyanodiethyl ether of ethylene glycol are saponified under these conditions to the amides in 80-85% yield. Only patent indications [8] exist in the literature on the synthesis of the β-cyanoethyl ether of β-butoxyethanol. We obtained this substance (in 66.6% yield) by the cyanoethylation of β-butoxyethanol (monobutyl ether of ethylene glycol) in the presence of a 2% aqueous potassium hydroxide solution. In the synthesis of this type of high-boiling β-alkoxypropionitriles it is necessary to carefully neutralize the reaction mixture; otherwise traces of alkali during distillation produce practically quantitative cleavage of the substance into its starting components.

All of the amides obtained by us are slow to crystallize, are readily soluble in water, and show quite a strong tendency to retain water, so that they are made completely anhydrous only after standing in a vacuum desiccator. The Hofmann rearrangement of β-butoxypropionamide gave β-butoxyethylamine in 19% yield. The reason for the low yield is the easy hydrolysis to β-butoxypropionic acid. Considerable tarring is observed in alcoholic medium, in which connection we were unable to isolate the β-butoxyethylamine.

During our work we made some modifications and improvements in the earlier described method [4] for the preparation of β-butoxypropionitrile.

EXPERIMENTAL

β-Butoxypropionitrile. In a 3-necked flask fitted with stirrer, dropping funnel and reflux condenser was placed 148 g of butyl alcohol and 100 ml 0.5% aqueous solution of caustic potash. 106 g acrylonitrile was then added drop-wise with stirring in the course of 1.5 hours and the mixture was heated 2 hours on a water bath at 80°. On cooling, the upper layer was separated off, neutralized with dilute acetic acid, dried with calcium chloride and vacuum distilled. Yield 200 g (78.7%) β-butoxypropionitrile:

B.p. 91-92° at 15 mm, n_D^{20} 1.4173, d_4^{20} 0.8895, MR_D 35.98; calc. 35.99. Literature data: b.p. 98° at 20 mm, n_D^{25} 1.4180, d_4^{25} 0.8863 [4].

After neutralization and vacuum fractionation, extraction of the aqueous layer with ether yielded 8-10 g more of nitrile; the total yield was 83-85%. In the distilling flask remained 3-4 g dicyanodiethyl ether with b.p. 160-166° at 8 mm, and a brown acrylonitrile polymer.

β-Cyanoethyl ether of β-butoxyethanol. To a mixture of 59 g monobutyl ether of ethyleneglycol and 25 ml 2% aqueous solution of caustic potash was added drop-wise 26.5 g acrylonitrile with stirring. The reaction evolved a slight amount of heat. After addition of all the acrylonitrile, the mixture was heated for 1 hour on a water bath at 70-80°, cooled, neutralized with dilute sulfuric acid, and set aside overnight, after which the upper layer was separated and dried with sodium sulfate. After 2 vacuum distillations, we obtained 57 g (66.6%) β-cyanoethyl ether of β-butoxyethanol:

B.p. 111-112° at 5 mm, n_D^{20} 1.4315, d_4^{20} 0.9500, MR_D 46.71; calc. 46.86. Literature data give: b.p. 130° at 10 mm [8].

β-Alkoxypropionamides. In a 3-necked flask fitted with stirrer and reflux condenser was placed 250 ml 3% hydrogen peroxide solution, 10.0 g β-butoxypropionitrile and into this was run ethyl alcohol until a homogeneous solution formed (mixture warmed up to 25-30° and slight amount of gas evolved). To the reaction mass was then added 2.5 ml 6N aqueous solution of caustic soda and the reaction mixture was heated with vigorous stirring for 4 hours on a water bath at 50-60°. The cooled mixture was precisely neutralized on litmus with dilute sulfuric acid and evaporated in a cup on a water bath. On standing in the air, the syrupy residue crystallized. After drying in a vacuum desiccator, β-butoxypropionamide (readily soluble in water, acetone, benzene) recrystallized from gasoline. Yield 11.0 g (96%). Oily to the touch, pearly flakes, m.p. 59°.

Found %: C 58.04, 57.90; H 10.58, 10.52. $C_7H_{15}O_2N$. Calculated %: C 57.90; H 10.41.

When acetone was added in place of alcohol, the yields fell to 48-60%. Use of a 6% solution of hydrogen peroxide gave only β-butoxypropionic acid and a portion of the nitrile returned unchanged. When alcohol was not added, the yield was 24%.

Similarly, 2.0 g β-methoxypropionitrile [3], 50 ml 3% hydrogen peroxide solution and 0.50 ml 6 N aqueous caustic soda solution yielded 2.3 g (98%) β-methoxypropionamide: M.p. 50° (from gasoline). Literature data give m.p. 49.6° [9].

From 2.0 g β-ethoxypropionitrile [3] was also obtained 2.3 g (97%) β-ethoxypropionamide: M.p. 50° (from gasoline). Literature data give m.p. 50.5° [9].

From 2.0 g β-cyanoethyl ether of β-butoxyethanol was obtained 2.0 g (90%) β-(β-butoxyethoxy)-propionamide with m.p. 20-20.5° (from gasoline).

Found %: N 7.32, 7.50. $C_9H_{19}O_3N$. Calculated %: N 7.42.

β,β'-Dicarbamidodiethyl ether of ethyleneglycol. The initial β,β'-dicyanodiethyl ether of ethyleneglycol was prepared by reacting 53 g acrylonitrile with 31 g ethyleneglycol in the presence of 2 ml 40% caustic soda solution (3 hours at 20-30° and 1 hour at 50-60°). After 2 vacuum distillations, we obtained 49.4 g (58.8%) substance with b.p. 183-185° at 8 mm, n_D^{25} 1.4468, which corresponded to the literature data [10]. To a mixture of 2.2 g β,β'-dicyanodiethyl ether of ethyleneglycol and 100 ml 3% hydrogen peroxide solution was added 35 ml alcohol and 1.0 ml 6 N caustic soda solution. The reaction mass was heated with stirring for 4 hours at 50-60°. The cooled transparent solution was neutralized on litmus with dilute sulfuric acid and evaporated on a water bath. After drying, the weight of residue was 2.49 g. After recrystallization from anhydrous alcohol, we obtained 2.3 g (86%) β,β'-dicarbamidodiethyl ether of ethyleneglycol: M.p. 123°. Literature data give m.p. 123° [11].

Found %: C 47.29, 47.21; H 7.93, 7.95; N 13.65, 13.55. $C_8H_{18}O_2N_2$. Calculated %: C 47.04; H 7.89; N 13.71.

Similarly, from 2.0 g β,β'-dicyanodiethyl ether [6], 100 ml 3% solution of hydrogen peroxide and 1.0 ml 6 N caustic soda solution was obtained 2.0 g (80%) β,β'-dicarbamidodiethyl ether: M.p. 146° (from anhydrous alcohol). Literature data give m.p. 146° [10].

β-Butoxypropionic acid. A mixture of 56 g β-butoxypropionitrile and 100 g concentrated hydrochloric acid was heated under reflux for 3 hours on a water bath at 70-80° and 0.5 hour at 100°. The upper layer was separated, the lower layer was extracted several times with acetone. The extracts were combined with the upper layer, the precipitate of ammonium chloride which came down was filtered off, then the acetone was driven off in vacuum and the residue was vacuum distilled twice. Yield 40 g (63%) β-butoxypropionic acid with an unpleasant odor:

B.p. 116° at 9 mm, n_D^{20} 1.4268, d_4^{20} 0.9933, MR_D 37.77; calc. 37.70. Literature data give b.p. 96-97.5° at 1 mm, n_D^{20} 1.4268, d_4^{20} 0.9929 [11].

After vacuum distillation in a stream of dry nitrogen, heating of 14 g β-butoxypropionic acid with 70 g thionyl chloride yielded 12 g (77%) β-butoxypropionyl chloride:

B.p. 62-63° at 6 mm, n_D^{20} 1.4303, d_4^{20} 1.0240, MR_D 41.50; calc. 41.42.

Found %: Cl 21.60, 21.72. $C_7H_{13}O_2Cl$. Calculated %: Cl 21.54.

After separation of ammonium chloride and steaming off the ether, the action of dry ammonia on an ethereal solution of the above acid chloride yielded β-butoxypropionamide with m.p. 59° (from gasoline). A mixed sample with the preparation, prepared by direct hydrolysis of the nitrile, was undepressed.

β-Butoxyethylamine. To a solution of 18.72 g caustic soda in 150 ml water, cooled to −3°, was added drop-wise 3.4 ml bromine with vigorous stirring. Then, without cessation of stirring, 10 g β-butoxypropionamide was gradually added. When all the amide had dissolved, the cooling mixture was removed and the solution was gradually heated to 70-80° (under reflux). After 30 minutes, the mixture was strongly alkalized and the amine driven off with steam into hydrochloric acid. The distillate was steamed to dryness; on cooling, the residue was decomposed with alkali under a layer of ether, extracted with ether, the combined extracts were dried with fused caustic potash and distilled. Yield 1.5 g (19%) of β-butoxyethylamine:

B.p. 148-150° at 735 mm, n_D^{20} 1.4186, d_4^{20} 0.8465, MR_D 34.93; calc. 34.96. Literature data give b.p. 148-150° [12].

The picrolonate of β-butoxyethylamine came down from the ether in the form of dark-yellow needles. After recrystallization from anhydrous alcohol:

M.p. 170° (with decomp.). Literature data give m.p. 172° [12].

The styphnate was in the form of bright-orange crystals with m.p 105° (from anhydrous alcohol).

Found %: N 15.40, 15.59. $C_{12}H_{18}O_9N_4$. Calculated %: N 15.48.

The benzenesulfonamide derivate was an oil, difficultly soluble in benzene, readily soluble in alcohol and ether.

When the rearrangement was carried out with an excess of bromine (10%), the yield fell to 12%. Similar results were obtained when soda was used instead of alkali or when the order of addition of the components was changed (amide, bromine, then alkali). When the quantity of alkali was reduced to 2 or 4 moles per 1 mole amide, no amine was obtained, but β-butoxypropionic acid separated out in a yield of about 60%.

SUMMARY

The synthesis of a number of β-alkoxypropionamides by the Radziszewski method of saponifying the corresponding nitriles was described.

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SYNTHESES WITH ACRYLONITRILE

XXVII. THE DIENE SYNTHESIS REACTION OF SUBSTITUTED ACRYLONITRILES

V.G. Yashunsky, A.P. Terentyev and Ya.G. Nekhlin

Together with reactivity tests with glycocoll and reduction by sodium in alcohol [1], we used the diene synthesis reaction to study the comparative reactivities of α,β-unsaturated nitriles.

As is known, acrylonitrile itself is an extremely active philodiene; data on whether other α,β-unsaturated nitriles – the homologs and analogs of acrylonitrile – show a similar capacity for diene addition are almost completely absent in the literature. Reference can be made only to the French patent of 1929 [2], where the reaction of the nitriles of crotonic and sorbic acids with 1,3-dimethylbutadiene and with cyclopentadiene is described, and also to the recently published study [3] on the reaction of methacrylic acid derivatives, and, in particular, the reaction of methacrylonitrile with butadiene and its analogs.

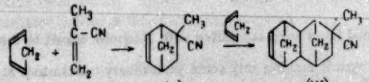
Our purpose in the present work was to study the comparative reactivity of α,β-unsaturated nitriles. As study subjects we selected crotonitrile, methacrylonitrile, cyclohexylideneacetonitrile and the nitriles of cinnamic and 1-cyclohexenecarboxylic acids, on the one hand, and cyclopentadiene, one of the more active symmetrical dienes, on the other.

All of the experiments were run under similar conditions: the mixture of components (nitrile: diene molar ratio = 1 : 1.5) was heated in a sealed tube in an oil bath at 160-165° for 8 hours; hydroquinone was introduced (about 0.01 g) to prevent polymerization.

In the case of crotonitrile we obtained the corresponding cyclic nitrile (I), identical with the earlier described product, in 60% yield, based on starting nitrile. In the reaction with methacrylonitrile the nitrile of 4-methyl-3,6-endomethylene-1-cyclohexene-4-carboxylic acid (II) was isolated in 78% yield. Together with it a substance was found to be present in the products, to which on the basis of its properties and analysis we consider it possible to assign the structure of a secondary condensation product (III).

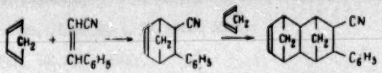
(I)

In the literature it is indicated that it is possible to form a similar dimeric product in the reaction of cyclopentadiene with allyl cyanide [4].



(II) (III)

The reaction of cyclopentadiene with the nitrile of cinnamic acid (consisting mostly of the trans form) under the same conditions gave two substances – the nitrile of 5-phenyl-3,6-endomethylene-1-cyclohexene-4-carboxylic acid (IV) (35.8%) and a small amount of secondary condensation product (V):



(IV) (V)

The reaction with cyclohexylideneacetonitrile and with the nitrile of 1-cyclohexenecarboxylic acid was run under analogous conditions. In both cases in working up the reaction mixture we were unable, to isolate any products other than the starting nitriles, and also the dimer and trimer of cyclopentadiene.

Since in all cases there occurred considerable tarring of the reaction mixture and the formation of high-boiling fractions, we decided to run the reaction of cyclopentadiene with crotonitrile, methacrylonitrile and the nitrile of cinnamic acid under milder conditions, and specifically, at 110° (the duration of reaction was 10 hours). In addition, these experiments should have served to verify the results obtained by us. To study the behavior of cyclohexylideneacetonitrile and of the nitrile of 1-cyclohexenecarboxylic acid under these conditions was meaningless.

In the case of the first three nitriles products were isolated that were identical with those obtained earlier, but in lower yields (see table); here we were unable to show the presence of secondary condensation products.

TABLE

Reaction of Cyclopentadiene with α,β-Substituted Unsaturated Nitriles

Nitrile	Yield of the reaction products with cyclopentadiene (in %)	
	Temperature 160°, duration of reaction 8 hours.	Temperature 110°, duration of reaction 10 hours
$CH_3CH=CH-CN$	60.8	27.0
$CH_2=C(CH_3)-CN$	78.0	75.2
$C_6H_5CH=CHCN$	35.8	20.5
	0	–
	0	–

The unexpectedly low yield of the reaction product with crotonitrile at 110° should be ascribed to the fact that the starting nitrile consisted of a mixture, containing approximately equal amounts of the cis and trans forms, whereas in the reaction at 160° we introduced crotonitrile that was quite rich in the cis form. Apparently, this also explains the fairly wide boiling range of the reaction product in the second case, probably also consisting of a mixture of geometric isomers.

We were unable to study the reaction of acrylonitrile with cyclopentadiene: here the ampoules containing the mixture, heated to 110°, exploded twice. However, on the basis of the data obtained by Bruson [5] it can in all probability be assumed that acrylonitrile should react quantitatively with this diene under our conditions.

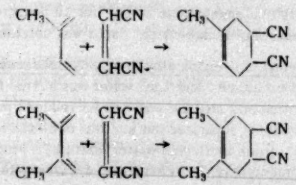
The cyclic nitriles obtained by us were saponified with alcoholic alkali to the corresponding acids.

Our experimental results permit making only some preliminary conclusions as to the relative reactivity of α,β-unsaturated nitriles when compared to the first member of the series – acrylonitrile – in the reaction with cyclopentadiene. Without doubt the hydrocarbon substituents impede the course of this reaction to a greater or less degree. In this connection the β-substituted nitriles (crotonitrile and cinnamonitrile) are considerably inferior to α-methylacrylonitrile in activity, whereas for a whole gamut of other reactions the reverse rule is observed. The nitriles with substitutents at both ends of the double bond proved to be the most passive. It is possible that here a large role is played by the fact that these nitriles belong to the alicyclic series.

Earlier one of us, together with A.N. Kost and S.M. Gurvich [6], had made a detailed study of the reaction of acrylonitrile with butadiene and its homologs and had synthesized several nitriles of the cyclohexene series; for this reason it seemed of interest to study the reaction of these dienes with fumaronitrile, one of the readily available and extremely active α,β-unsaturated dinitriles, and obtain the corresponding cyclic dinitriles.

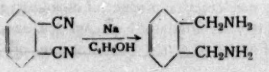
The reaction of fumaronitrile with butadiene is described in the literature, but at the same time it is indicated that the running of it is accompanied by considerable difficulties. Thus, Ziegler [7] was able to achieve a 76% yield of the dinitrile of 1-cyclohexene-4,5-dicarboxylic acid only after passing butadiene into a boiling toluene solution of fumaronitrile for 427 hours; however, in this connection he was unable to avoid considerable tarring of the reaction mixture.

We ran our experiments in sealed glass ampuls under heating at 110° for 24 hours. As solvent we selected toluene. To prevent polymerization we introduced hydroquinone into the reaction mixture. From a whole series of experiments it was found that even with a 2-fold excess of butadiene the corresponding dinitrile is obtained in nearly quantitative yield. The reaction of fumaronitrile with isoprene and with 2,3-dimethylbutadiene proceeded smoothly:



In all cases the formation of a rubberlike copolymer in an amount equal to 2-3% of the final product was observed.

The saponification of the dinitriles of 1-cyclohexene-4,5-dicarboxylic and 1-methyl-1-cyclohexene-4,5-dicarboxylic acids gave the corresponding acids and anhydrides. The dinitrile of 1-cyclohexene-4,5-dicarboxylic acid was also reduced with sodium in butyl alcohol; here only one base was isolated. Analysis and the presence of primary amino groups, shown by qualitative reactions, permit assigning the structure of 4,5-di-(aminomethyl)-1-cyclohexene to this compound:



The presence of a double bond in the diamine was shown by its reaction with permanganate. A.A. Petrov and N.P. Sopov [8], who reduced the nitrile of 1-cyclohexene-4-carboxylic acid by the same method, also obtained an unsaturated amine. The diamine obtained by us is a colorless liquid with a characteristic odor; it readily absorbs carbon dioxide from the air. Apparently, this can serve to explain the considerable difference shown for the found and calculated values of the molecular refraction.

EXPERIMENTAL*

Reaction of α,β-unsaturated nitriles with cyclopentadiene

Crotonitrile. A mixture of 7 g crotonitrile (b.p. 107-113°, n_D^{20} 1.4220) and 10.31 g cyclopentadiene was heated in a sealed ampul on an oil bath for 8 hours at 160°. The red-brown reaction mixture was vacuum distilled. 8.4 g (60.8%, based on nitrile) nitrile of 5-methyl-3,6-endomethylene-1-cyclohexene-4-carboxylic acid (I) was isolated:

B.p. 88-91° at 11 mm, n_D^{20} 1.4870, d_4^{20} 0.9832, MR_D 38.96; calc. 38.71. Literature data give b.p. 87-88.5° at 12 mm [2].

*Preparation of the unsaturated nitriles was described in one of the preceding communications [1].

On heating crotonitrile (b.p. 111-115.5°, n_D^{20} 1.4230) with cyclopentadiene in a sealed ampul for 10 hours at 110°, a yield of 27% cyclic nitrile (I) was obtained with b.p. 82-95° at 13 mm (the main bulk distilled over at 89-93°), n_D^{20} 1.4880.

Saponification of nitrile of 5-methyl-3,6-endomethylene-1-cyclohexene-4-carboxylic acid.* A mixture of 3 g nitrile and 7 g caustic soda solution in 7 ml water and 20 ml alcohol was heated until evolution of ammonia ceased (26 hours). The alcohol was driven off in vacuum, the residue was neutralized with sulfuric acid and extracted with ether. Vacuum distillation yielded an oil:

B.p. 125.5° at 8 mm, n_D^{20} 1.4913, d_4^{20} 1.0890, MR_D 40.49; calc. 40.43. Literature data give b.p. 137-139° at 18 mm [9].

Methacrylonitrile. 8.5 g methacrylonitrile was heated with 12.5 g cyclopentadiene at 160° for 8 hours. Fractionation of the reaction mixture yielded two fractions. From the 1st (14.7 g), which came over in the interval 40-71° (at 6 mm), a repeated distillation yielded 13.2 g (78.0%) nitrile of 4-methyl-3,6-endomethylene--1-cyclohexene-4-carboxylic acid (II) with b.p. 67-69° at 6 mm and m.p. 55°. From the 2nd fraction (1.0 g, 71-115° at 6 mm) treatment with alcohol yielded 0.3 g secondary condensation product of methacrylonitrile with cyclopentadiene (III); fine needles from alcohol, m.p. 117.5-118°.

Found %: C 84.55, 84.54; H 8.68, 8.59. $C_{14}H_{17}N$. Calculated %: C 84.37; H 8.60.

On heating methacrylonitrile with cyclopentadiene at 110° for 10 hours, only a 75.2% yield of nitrile of 4-methyl-3,6-endomethylene-1-cyclohexene-4-carboxylic acid was obtained, b.p. 84° at 14 mm.

Saponification of nitrile of 4-methyl-3,6-endomethylene-1-cyclohexene-4-carboxylic acid (II). A mixture of 2 g nitrile, 5 g caustic soda, 20 ml alcohol and 7 ml water was heated for 140 hours under reflux. Alcohol was driven off from the yellow solution and also the water under reduced pressure, and the residue was treated with ether. A salt in the form of a suspension separated out and was neutralized with sulfuric acid, after which an acid came down with m.p. 78-78.5° (from an alcohol-water mixture). From the ethereal solution was isolated the amide of 4-methyl-4,6-endomethylene-1-cyclohexene-4-carboxylic acid with m.p. 150.5-151° in a sealed capillary (from water); it was sublimable.

Found %: N 8.99, 9.00. $C_9H_{13}ON$. Calculated %: N 9.26.

Nitrile of cinnamic acid. 12.9 g nitrile of cinnamic acid was heated with 9.9 g cyclopentadiene in an ampul for 8 hours at 160°. The following fractions were obtained upon vacuum distillation: 1st, b.p. up to 120° at 3 mm, 9.16 g; 2nd, b.p. 120-160° at 3 mm, 9.78 g; 3rd, b.p. 160-180° at 3 mm, 1.64 g.

The 1st fraction contained dicyclopentadiene and initial nitrile. A repeated distillation of the 2nd fraction yielded 7.0 g (35.8%) nitrile of 5-phenyl-3,6-endomethylene-1-cyclohexene-4-carboxylic acid (IV): b.p. 141-142° at 2 mm, n_D^{20} 1.5645, d_4^{20} 1.0902, MR_D 58.20; calc. 58.29.

The 3rd fraction was a secondary condensation product of cinnamic acid nitrile with cyclopentadiene (V). When the reaction was carried out at 110°, the nitrile of 5-phenyl-3,6-endomethylene-1-cyclohexene-4-carboxylic acid was obtained in a yield of 20.5%; b.p. 136-142° at 2 mm, n_D^{20} 1.5659.

Saponification of condensation products of cinnamic acid nitrile with cyclopentadiene. When the nitrile of 5-phenyl-3,6-endomethylene-1-cyclohexene-4-carboxylic acid was boiled with aqueous alcoholic solution of alkali an acid was obtained with m.p. 111-111.5° (from alcohol).

Found %: C 78.54, 78.47; H 6.77, 6.61. $C_{14}H_{14}O_2$. Calculated %: C 78.47; H 6.58.

Saponification of the substance with b.p. 160-180° at 3 mm by the same method resulted in a solid product being obtained, which after repeated crystallizations from alcohol, had m.p. 229° in a sealed capillary (sublimes).

Found %: C 81.55, 81.62; H 7.59, 7.78. $C_{19}H_{20}O_2$. Calculated %: C 81.39; H 7.19.

Nitrile of cyclohexene-1-carboxylic acid. A mixture of 9.1 g nitrile and 8.45 g cyclopentadiene was heated at 160° for 8 hours. Aside from the initial nitrile and cyclopentadiene dimer, distillation of the reaction products yielded a substance which after recrystallization from methyl alcohol, had m.p. 65-65.5°. A Lassen test for nitrogen proved negative.

Found %: C 90.73, 90.91; H 9.00, 9.28. Trimer of cyclopentadiene $C_{15}H_{18}$. Calculated %: C 90.85; H 9.15.

*Saponification of nitriles was carried out by A.A. Petrov-N.P. Copov's method [8].

A mixed melting test with the trimer of cyclopentadiene, separated from the flask in which decomposition of the cyclopentadiene dimer to the monomer was carried out, gave no depression. According to the literature data, the trimer of cyclopentadiene has m.p. 60° [10].

Cyclohexylideneacetonitrile. No other substances except initial nitrile, dimer and trimer of cyclopentadiene were detected in the reaction products of cyclohexylideneacetonitrile and cyclopentadiene (3 hours, 160°). About 2 g trimer of cyclopentadiene with m.p. 59° was obtained.

Reaction of fumaronitrile with dienes.

Fumaronitrile was obtained by dehydration of the diamide of fumaric acid by means of phosphoric anhydride [11] and P_2O_5 in mixture with powdered aluminum [12]. In both cases the yield of dinitrile reached 60-65%; m.p. 96-97° (from toluene), which corresponds to the literature data.

A mixture of 40 ml anhydrous toluene, saturated with strong cooling of 16 g commercial butadiene, 11.54 g fumaronitrile and 0.01 g hydroquinone was heated in a sealed ampul for 24 hours at 110°. The precipitate which came down on cooling was recrystallized from anhydrous alcohol. Yield 18.5 g (94.7%) dinitrile of 1-cyclohexene 4,5-dicarboxylic acid with m.p. 124-124.5° (white flakes). Literature data give m.p. 125° [7]. Moreover, about 0.3 g rubberlike polymer was obtained. Increase of the excess of butadiene to a 6- or 15-fold excess did not increase the yield of cyclic dinitrile and brought about only increased formation of polymer.

Saponification of dinitrile of 1-cyclohexene-4,5-dicarboxylic acid was carried out as described previously by heating with aqueous alcoholic solution of alkali for 2 hours. The acid, recrystallized three times from a water-alcohol mixture, had m.p. 165-166° in a sealed capillary (sublimes). Heating of the acid with an excess of acetic anhydride (1:5) for 20 minutes yielded the anhydride of 1-cyclohexene-4,5-dicarboxylic acid with m.p. 92-93° (from ether). The acid and anhydride that were obtained, on the basis of their melting points, apparently belong to the cis category [13]; such a conclusion has not been reached as yet regarding the configuration of the nitrile.

A mixture of 4 g fumaronitrile, 6.8 g isoprene with hydroquinone and 15 ml anhydrous toluene was heated in a sealed ampul for 24 hours at 110°. After the toluene was driven off, the residue was recrystallized from anhydrous alcohol; yield 6.83 g (91.5%) dinitrile of 1-methyl-1-cyclohexene-4,5-dicarboxylic acid, m.p. 70-70.5°. Saponification of this dinitrile yielded an oil which was quite readily soluble in water and which was converted to the solid anhydride upon vacuum distillation; after recrystallization from acetic anhydride, it had m.p. 138.5-139.5° in a sealed capillary (sublimes). The literature gives data only on the condensation product of isoprene with maleic anhydride, i.e., for the cis-anhydride, namely, with m.p. 63-64° [14].

Found %: C 64.88, 64.91; H 6.04, 6.09. $C_9H_{10}O_3$. Calculated %: C 65.05; H 6.07.

Heating of a mixture of fumaronitrile and 2,3-dimethylbutadiene in toluene yielded the dinitrile of 1,2-dimethyl-1-cyclohexene-4,5-dicarboxylic acid in the form of long transparent prisms from anhydrous alcohol with m.p. 120.5-121.5° in a sealed capillary (sublimes).

Reduction of dinitrile of 1-cyclohexene-4,5-dicarboxylic acid. To a solution of 12 g dinitrile in 600 g anhydrous butyl alcohol was added 32.4 g sodium and the mixture was boiled until the metal was completely dissolved. Treatment of the reaction products yielded 4.16 g colorless liquid of basic character with b.p. 115-119° at 9 mm. This diamine was finally isolated in the form of the hydrochloride (0.75 g) from the mass before distillation and from the residue after distillation. After a repeated distillation: b.p. 116.5° at 10 mm, n_D^{20} 1.5194, d_4^{20} 1.0205, MRD 41.73; calc. 43.33.

The yield of diamine was 36.6%.

The diamine dihydrochloride was prepared by passage of dry hydrogen chloride into an alcoholic solution of the diamine, m.p. 265-268° in a sealed capillary (decomp.).

Found %: N 13.07, 13.06. $C_8H_{18}N_2Cl_2$. Calculated %: N 13.21.

The dibenzyl derivative had m.p. 177.5-178.5° (from alcohol) in a sealed capillary (sublimes).

The dipicrate (from benzene) was a fluffy precipitate which deliquesced and darkened in air.

SUMMARY

1. The comparative reactivity of a number of α,β-unsaturated nitriles in the diene synthesis reaction was studied on the example of their reaction with cyclopentadiene.

2. A method was developed for obtaining the dinitriles of 1-cyclohexene-4,5-dicarboxylic acids by the reaction of fumaronitrile with butadiene and its homologs.

3. The reduction of the dinitrile of 1-cyclohexene-4,5-dicarboxylic acid with sodium in alcohol gives the corresponding diamine.

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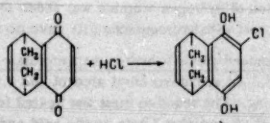
QUINONES

IX. THE REACTION OF 5,8-ENDOETHYLENE-1,4-NAPHTHOQUINONE WITH HYDROGEN CHLORIDE AND WITH ACETOACETIC ESTER

A.N. Grinev, A.B. Terentyev and A.P. Terentyev

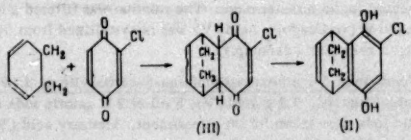
5,8-Endoethylene-1,4-naphthoquinone (I) was first obtained by Diels and Alder [1] via the oxidation of the corresponding hydroquinone with ferric chloride. Recently we developed [2] a convenient synthesis of quinone (I) via the oxidation of 5,8-endoethylenenaphthohydroquinone with potassium bromate in acid medium.

In the present work we studied the reaction of this quinone (I) with hydrogen chloride:



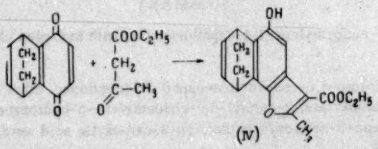
(I) (II)

The reaction was run under conditions similar to those described earlier [3]. The structure of the hydroquinone (II) was proved by the counter synthesis:



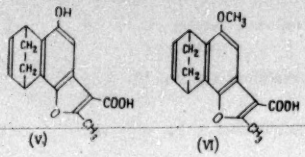
(III) (II)

5,8-Endoethylene-1,4-naphthoquinone (I) also reacts with acetoacetic ester; here the ethyl ester of 2-methyl-6,9-endoethylene-5-hydroxynaphthofuran-3-carboxylic acid (IV) is formed.



(IV)

The saponification of ester (IV) gave 2-methyl-6,9-endoethylene-5-hydroxynaphthofuran-3-carboxylic acid (V). The methylation of acid (V) gave 2-methyl-6,9-endoethylene-5-methoxynaphthofuran-3-carboxylic acid (VI)



(V) (VI)

EXPERIMENTAL

1. 2-Chloro-5,8-endoethylenenaphthohydroquinone (II). To a solution of 1 g hydrogen chloride in 20 ml ether (prepared by saturation in the cold) was added 0.9 g quinone (I) in portions with cooling and vigorous mixing. After driving off the ether and recrystallization from glacial acetic acid, 1 g of chlorohydroquinone (II) was obtained. The yield was quantitative. White crystals. M.p. 155°.

Found %: C 64.12, 64.31; H 4.88, 4.87. $C_{12}H_{11}O_2Cl$. Calculated %: C 64.72; H 4.98.

2. Adduct (III) of chloroquinone with cyclohexadiene. A solution of 3 g chlorobenzoquinone in 20 ml benzene was mixed with 6 g cyclohexadiene. After standing for 2 days, the benzene was driven off. Yield 4 g of adduct (III) (87%). Yellow crystals with m.p. 78-79° (from ethanol).

Found %: C 64.74, 64.76; H 5.10, 5.22. $C_{12}H_{11}O_2Cl$. Calculated %: C 64.72; H 4.98.

3. Isomerization of adduct (III). 1.6 g of adduct (III) was dissolved with heating in 3 ml glacial acetic acid and 2-3 drops of acetic acid solution of hydrogen bromide was added to the solution. Yield 1.1 g of white crystals with m.p. 153-154°. A mixing test with hydroquinone (II) gave no melting point depression.

4. Ethyl ester of 2-methyl-6,9-endoethylene-5-hydroxynaphthofuran-3-carboxylic acid (IV). To a solution of 4 g anhydrous zinc chloride in 6.5 ml anhydrous ethyl alcohol and 8.5 ml acetoacetic ester was added 5 g of quinone (I) in portions with mixing. The reaction mass was heated for 30 minutes on a water bath. 7 g of ester (IV) was obtained in the form of white flakes (from acetic acid and gasoline). Yield 87.5%. M.p. 192-193°. Found %: C 72.52, 72.65; H 6.62, 6.59. $C_{18}H_{16}O_4$. Calculated %: C 72.50; H 6.08.

5. 2-Methyl-6,9-endoethylene-5-hydroxynaphthofuran-3-carboxylic acid (V). 2.5 g ester (IV) was heated for 15 minutes with a solution of 1.75 g caustic soda in 25 ml anhydrous alcohol. 25 ml water was added and the reaction mass was heated for 20 minutes more. The solution was filtered and acidified with 2 N hydrochloric acid until an acid reaction (on Congo). Acid (V) was recrystallized from 50% alcohol. Yield 1.7 g white crystalline substance with m.p. 233° (decomp.).

6. 2-Methyl-6,9-endoethylene-5-methoxynaphthofuran-3-carboxylic acid (VI). Methylation of acid (V) was carried out by the usual method. 1.1 g acid (V), 6 ml of 2 N caustic soda solution, 1 ml dimethyl sulfate and 0.9 g solid caustic soda were taken for the experiment. Methoxy acid (VI) was sublimed at 190-200°. Yield 0.8 g (70%). M.p. 272° (with decomp).

Found %: C 71.56, 71.45; H 5.50, 5.65. $C_{17}H_{16}O_4$. Calculated %: C 71.81; H 5.67.

SUMMARY

1. The reaction of 5,8-endoethylene-1,4-naphthoquinone with hydrogen chloride and with acetoacetic ester was studied.

2. The compounds 2-chloro-5,8-endoethylenenaphthohydroquinone, ethyl 2-methyl-6,9-endoethylene-5-hydroxynaphthofuran-3-carboxylate, 2-methyl-6,9-endoethylene-5-hydroxynaphthofuran-3-carboxylic acid and 2-methyl-6,9-endoethylene-5-methoxynaphthofuran-3-carboxylic acid were prepared.

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HIGH-MOLECULAR COMPOUNDS

XCV. THE POLYESTERS OF THIODIVALERIC ACID

V.V. Korshak and S.V. Vinogradova

For the purpose of studying the dependence of polyester properties on the structure of the polymeric chain and the nature of the starting substances we investigated the influence of the structure of the starting glycols on the properties of polyesters [1-7]. We prepared and studied the polyesters of polymethylene glycols [1-6] having the general formula $HO(CH_2)_nOH$ with n = 2,3,4,5,6,10,20, and also glycols of the type of diethylene glycol and triethylene glycol, i.e., glycols containing straight ether linkages in their molecule [4,5], and finally we studied the glycols with side-chain methyl groups [7,4] (propylene glycol; 1,3-butanediol). The influence of the structure of the dicarboxylic acids on the properties of the polyesters derived from them was less extensively studied, inasmuch as only the acids of the homologous series $HOOC(CH_2)_nCOOH$ were used. For the purpose of expanding the data in this direction we began a study of the influence of the structure of the starting dicarboxylic acids on the properties of the polymers derived from them. As our first study subject we selected the polyesters of thiodivaleric acid, the preparation of which was realized by the method used by us to prepare the polyesters of oxalic and malonic acids [2-5].

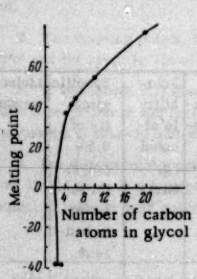

Fig. 1. Variation in the melting points of thiodivaleric acid polyesters as a function of the number of carbon atoms in the glycol molecule.

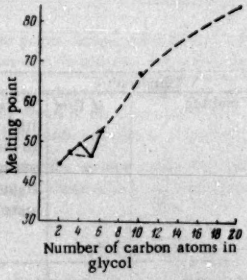

Fig. 2. Variation in the melting points of azelaic acid polyesters as a function of the number of carbon atoms in the glycol molecule.

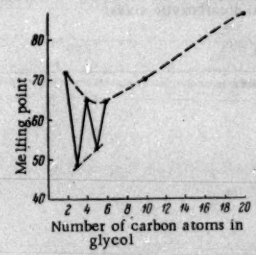

Fig. 3. Variation in the melting points of sebacic acid polyesters as a function of the number of carbon atoms in the glycol molecule.

Proceeding from the data in Table 1, and also from the graphical representation of the change in the melting points of the thiodivaleric acid polyesters as a function of the number of carbon atoms in the starting glycol, shown in Fig. 1, it can be seen that in measure with increase in the length of the methylene chain in the starting glycol the melting points of the polyesters smoothly increase from -38° for the polyester of ethylene glycol to 76° for the polyester of eicosamethylene glycol. A zigzag nature for the melting point changes, so characteristic for other dicarboxylic acids, fails to exist in the present case. If we investigate the manner in

which the melting points change in the polyester series of the neighboring polymethylene dicarboxylic acids, and specifically, those of azelaic and sebacic acids, we can see that here the curves for the melting point changes fail to have as smooth a character (Figs. 2 and 3) as for the polyesters of thiodivaleric acid, where the influence of the "evenness factor" is greatly diminished. The melting points of the thiodivaleric acid polyesters show lower values than do the melting points of the corresponding polyesters of azelaic and sebacic acids. Thus, the polyester derived from thiodivaleric acid and ethylene glycol is a liquid with m.p. -38°; polyethylene azelate and polyethylene sebacate are solids with respective m.p. of 44 and 72°; the polyester from thiodivaleric acid and trimethylene glycol melts at -39°, polytrimethylene glycol azelate melts at 47°, polytrimethylene glycol sebacate melts at 49°, etc. The diminished influence of the "evenness factor" [4] and the lower melting points shown by the thiodivaleric acid polyesters when compared with the polyesters of sebacic and azelaic acids can apparently be explained by the presence of the -S-bond in the starting dicarboxylic acid, which evidently behaves in the same manner as a straight ether linkage in the glycol molecule, facilitating an increase in the flexibility of the polymeric chain due to free rotation of the methylene groups with respect to this bond, which produces a reduction in the melting point of the polymer. The polyesters derived from thiodivaleric acid and glycols, containing side-chain methyl groups and a straight ether linkage in their chain (propylene glycol, 1,3--butanediol, diethylene glycol, triethylene glycol), are liquids with close melting points ranging from -39 to -42°. For the solid polyesters of thiodivaleric acid (from the polyester of tetramethylene glycol to the polyester of eicosamethylene glycol) a Hoppler consistometer was used to determine (under a load of 1 kg) the flow points and the temperatures of transition into the viscous liquid state. The character of the changes in these constants as a function of the glycol used is retained in the same manner as for the changes in the melting points of these polyesters. The temperature interval between the flow point and the temperature of transition into the viscous liquid state for the polyesters of pentamethylene glycol, hexamethylene glycol and decamethylene glycol is 1°, for the polyester of eicosamethylene glycol it is 2.5°, and for the polyester of trimethylene glycol it is 3.5°. On the basis of these data it can be assumed that the solid polyesters of thiodivaleric acid are crystalline. The temperatures of transition into the viscous liquid state are lower for the polyesters of thiodivaleric acid than for the corresponding polyesters of sebacic and azelaic acids. Thus, for example, the temperature of transition into the viscous liquid state for the polyester of thiodivaleric acid and tetramethylene glycol is 39°, for polytetramethylene azelate it is 51°, for polytetramethylene sebacate it is 69°, for the polyester of thiodivaleric acid and decamethylene glycol it is 59°, for polydecamethylene sebacate it is 78°, etc. The melting points, flow points and temperatures of transition into the viscous liquid state for some of the sebacic acid polyesters are given in Table 2. A reduction in the temperatures of transition into the viscous liquid state for the thiodivaleric acid polyesters indicates a greater flexibility of the polymeric chains in these polyesters when compared with the polyesters of normal dicarboxylic acids.

TABLE 1

Polyester	Temperature			Solubility in alcohol (g/liter)	Specific viscosity of 0.5% polyester solution in benzene	Molecular weight
	of melting	of flow	of transition into the viscous liquid state			
$-CO(CH_2)_4S(CH_2)_4COO(CH_2)_2O-$	-38 to -34°	–	–	6.2	0.095	3530
$-CO(CH_2)_4S(CH_2)_4COO(CH_2)_3O-$	-39 to -36	–	–	6.3	0.075	2760
$-CO(CH_2)_4S(CH_2)_4COO(CH_2)_4O-$	37-38	42.5°	39°	10.0	0.13	4720
$-CO(CH_2)_4S(CH_2)_4COO(CH_2)_5O-$	40-42	44	43	11.35	0.071	2580
$-CO(CH_2)_4S(CH_2)_4COO(CH_2)_6O-$	44-46	46	44	4.65	0.19	6603
$-CO(CH_2)_4S(CH_2)_4COO(CH_2)_{10}O-$	54-57	60.5	59	3.3	0.15	5200
$-CO(CH_2)_4S(CH_2)_4COO(CH_2)_{20}O-$	76-79	85.5	83	0.93	0.21*	3560
$-CO(CH_2)_4S(CH_2)_4COOCH_2CHO-$ (CH3)	-39 to -34	–	–	15.7	0.05	1970
$-CO(CH_2)_4S(CH_2)_4COOCH_2CH_2CHO-$ (CH3)	-41 to -36	–	–	14.9	0.058	2250
$-CO(CH_2)_4S(CH_2)_4COOCH_2CH_2OCH_2CH_2O-$	-39 to -35	–	–	7.95	0.054	1960
$-CO(CH_2)_4S(CH_2)_4CO(OCH_2CH_2)_3O-$	-42 to -37	–	–	11.05	0.045	1600

*In cresol.

TABLE 2

Polyesters	Temperature			Specific viscosity of 0.5% polyester solution in benzene	Molecular weight
	of melting	of flow	of transition into the viscous liquid state		
$-CO(CH_2)_8COOCH_2CH_2O-$	74-77°	80.5°	79°	0.135	4700
$-CO(CH_2)_8COO(CH_2)_3O-$	49-51	56	54	0.062	2150
$-CO(CH_2)_8COO(CH_2)_4O-$	65-67	69	68	0.12	4130
$-CO(CH_2)_8COO(CH_2)_5O-$	53-57	55	54	0.088	2290
$-CO(CH_2)_8COO(CH_2)_6O-$	69-68	72	70	0.135	4560
$-CO(CH_2)_8COO(CH_2)_{10}O-$	75-77	80	78	0.225	7400
$-CO(CH_2)_8COO(CH_2)_{20}O-$	91-92	93	92	0.24*	4110
$-CO(CH_2)_8CO(OCH_2CH_2)_2O-$	45-47	50	48	0.1	3460
$-CO(CH_2)_8CO(OCH_2CH_2)_3O-$	33-35	39	26	0.11	3740

*In cresol.

Determination of the alcohol solubilities of the thiodivaleric acid polyesters revealed that the solubility values are comparatively low, ranging for the different polymers from 0.93 to 15.7 g/liter.

In conclusion the authors wish to thank R.Kh. Freidlina for graciously placing the thiodivaleric acid at their disposal.

SUMMARY

1. Polyesters derived from thiodivaleric acid and glycols of general formula $HO(CH_2)_nOH$ with n = 2,3, 4,5,6,10 and 20, and also propylene glycol, 1,3-butanediol, diethylene glycol and triethylene glycol, were prepared.

2. The melting points, flow points, temperatures of transition into the viscous liquid state, solubilities in alcohol and the specific viscosities of 0.5% solutions in benzene were determined for the obtained polyesters.

3. It was shown that the introduction of the sulfide bond into the molecule of a dicarboxylic acid (sebacic) leads to a reduction in the melting points of the polyesters derived from it when compared with the corresponding polyesters of sebacic and azelaic acids, and also to a diminished importance of the "evenness factor".

4. For the purpose of comparing the melting points, flow points and temperatures of transition into the viscous liquid state of the polyesters of thiodivaleric and sebacic acids the data for these constants are given for a number of sebacic acid polyesters.

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*T.p. = C.B. Translation pagination

HIGH-MOLECULAR COMPOUNDS

XCVI. SYNTHESIS AND POLYMERIZATION OF 4-VINYLPHENYLETHANE

G.S. Kolesnikov, V.V. Korshak and I.P. Kulyulin

4-Vinyldiphenylethane is a monomer that up to now has not been described in the literature; its synthesis and polymerization are of undoubted interest for the reason that it is not clear how the introduction of the β-phenethyl radical in the para position of the styrene molecule will influence the properties of the polymer, in particular, the temperature of transition into the viscous liquid state. It is known that increase in the chain length of the alkyl substituent in p-alkylstyrenes leads to a reduction in the softening temperatures of the polymers that are obtained by the polymerization of these monomers [1]. At the same time there are statements in the literature [2] that the polymer of 4-vinyldiphenylethane, obtained by the dehydration of 4-(α-hydroxyethyl)-diphenylethane, fails to melt when heated to 300°, on the basis of which it can be concluded that the introduction of a β-phenethyl group into styrene raises the softening temperature of its polymer.

We synthesized 4-vinyldiphenylethane in the following manner. Diphenylethane, obtained by reacting benzene with dichloroethane in the presence of aluminum chloride [3], was brominated in the presence of iron [4] and gave 4-bromodiphenylethane. The structure of the 4-bromodiphenylethane was proved by its oxidation with potassium permanganate to benzoic and p-bromobenzoic acids. From 4-bromodiphenylethane we obtained the organomagnesium compound in the usual manner, the reaction of which with ethylene oxide gave 4-(β-hydroxyethyl)diphenylethane. The structure of the latter was proved by its oxidation to a mixture of benzoic and terephthalic acids. We also prepared the previously unknown esters of 4-(β-hydroxyethyl)diphenylethane with acetic and benzoic acids. The heating of 4-(β-hydroxyethyl)diphenylethane with potassium hydroxide in vacuo gave the previously unknown 4-vinyldiphenylethane.

The polymerization of 4-vinyldiphenylethane and its copolymerization with methyl methacrylate and with styrene was run in the presence of 0.3% benzoyl peroxide under heating in evacuated sealed ampuls. For the polymers and copolymers obtained in this manner we determined the temperature of transition into the viscous liquid state (using a Hoppler consistometer and a load of 1 kilogram /cm²) and the specific viscosity of their benzene solutions (0.3 g of polymer in 100 ml of benzene). The obtained results are given in the table.

TABLE

Properties of the Polymers and Copolymers of 4-Vinyldiphenylethane

Composition of the starting mixture of monomers (in mole %)			Temperature of transition into the viscous liquid state	Specific viscosity of the polymer solution in benzene at 20°
4-Vinyldiphenylethane	methyl methacrylate	styrene		
100.0	0.0	–	44°	0.127
81.3	18.7	–	54	0.131
49.5	50.5	–	63	0.547
24.4	75.6	–	88	0.652
0.0	100.0	–	110	0.683
76.4	–	23.6	53	0.129
50.0	–	50.0	68	0.136
25.6	–	74.4	78	0.193
0.0	–	100.0	91	0.269

From the data in the table it can be seen that the temperature for the transition of the 4-vinyldiphenylethane polymer into the viscous liquid state is considerably lower than it is for either polystyrene or polymethyl methacrylate. For the copolymers of 4-vinyldiphenylethane with either styrene or methyl methacrylate the temperature of transition into the viscous liquid state rises in measure with decrease in the amount of 4-vinyldiphenylethane in the starting mixture of monomers. As a result, the data of Yura and Oda [2] on the high melting point of the 4-vinyldiphenylethane polymer does not agree with fact.

The reduction in the temperature of transition into the viscous liquid state when the β-phenethyl radical is introduced into the benzene ring of the elementary polystyrene unit in the para position can be explained by the fact that due to the larger volume of the substituent the interaction between the individual polymer molecules is weakened, which is manifested in a reduction of the temperature of transition into the viscous liquid state. A reduction in the number of such substituents as the result of copolymerization with another monomer, for example with styrene, leads to the situation that interaction between the polymer molecules is weakened in less degree, as a result of which the temperature of transition into the viscous liquid state rises.

EXPERIMENTAL

4-Bromodiphenylethane [2]. In a four-necked flask fitted with stirrer, reflux condenser, thermometer reaching almost to the bottom of the flask and dropping funnel, was placed 485 g diphenylethane, prepared from benzene and dichloroethane [3], and 10 g iron filings or shavings. The contents of the flask were heated to 55° and 421 g dry bromine was added with stirring in the course of 2 hours; 30 minutes after addition of bromine had started, the temperature in the flask was lowered to 40°. After all the bromine had been added, the contents of the flask were heated for 1.5 hours on a boiling water bath and set aside overnight. The reaction mixture was dissolved in 300 ml benzene and the benzene solution was washed twice with 10% alkali solution and then 4 times with water. The benzene solution was dried with calcium chloride, the benzene was driven off and the residue was vacuum-distilled. Yield 295-305 g of crude 4-bromodiphenylethane (36.5-38%) with b.p. 141-143° (3-4 mm). A repeated distillation gave 250-260 g 4-bromodiphenylethane with b.p. 145-147° (4 mm), d_{20}^{20} 1.2827, n_D^{20} 1.5942.

Found %: C 64.44, 64.54; H 5.10, 5.01; Br 30.12, 29.93. $C_{14}H_{13}Br$. Calculated %: C 64.38; H 5.02; Br 30.60.

Oxidation of 4-bromodiphenylethane. 5 g of 4-bromodiphenylethane, 500 ml water, 1 g caustic soda and 4 g potassium permanganate were boiled until the violet color disappeared and then potassium permanganate was added in 2 g portions until oxidation was complete. The mixture of acids was precipitated from alkaline solution by the usual method and set aside overnight. The crystals which came down were filtered off and the filtrate was extracted 8 times with benzene. The benzene extracts were combined, benzene was driven off from them and the residue was combined with the crystals. The mixture of solid products was extracted twice with boiling distilled water and the insoluble portion was filtered off. The crystals which came down from the aqueous extract had m.p. 120-121° and gave no depression in mixture with known benzoic acid. The oxidation products that were insoluble in water, after drying, had m.p. 249-250°; according to literature data, p-bromobenzoic acid has m.p. 251-253° [6].

Found %: C 42.09, 42.02; H 2.73, 2.66; Br 39.20, 38.88. $C_7H_5O_2Br$. Calculated %: C 41.82; H 2.52; Br 39.40.

4-(β-Hydroxyethyl)diphenylethane. In a 500 ml 3-necked flask fitted with stirrer, reflux condenser, thermometer and dropping funnel was placed 15.5 g magnesium and 200 ml dry ether. One fifth of a solution of 166 g 4-bromodiphenylethane in 150 ml dry ether was added to the flask and after the reaction started, the remainder of the 4-bromodiphenylethane solution was added; the reaction mixture was then boiled for 3 hours with stirring. The reaction mixture was cooled to -12° and a solution of 35 g ethylene oxide in 100 ml dry ether, previously cooled to -16°, was slowly added with stirring to the reaction mixture. During addition, the solution was held at -12 to -18°. When the reaction was complete, the organomagnesium compound was decomposed with 100 ml of 30% ammonium chloride solution, the ethereal layer was separated off and dried with anhydrous magnesium sulfate. The ether was driven off from the solution and the residue was vacuum-distilled, the fraction with b.p. 179-181° (4 mm) was collected. After one more vacuum-distillation, 63-70 g (44-49%) of 4-(β-hydroxyethyl)diphenylethane was obtained. After recrystallization from benzene, it had m.p. 62.5-63.5°; a repeated recrystallization failed to raise the melting point. The literature data [5] give b.p. 172° (3 mm), m.p. 67-68°.

Found %: C 84.81, 84.71; H 8.04, 7.93. M 224,227,222 (Rast). $C_{16}H_{18}O$. Calculated %: C 84.91; H 8.02; M 226.3.

Oxidation of 4-(β-hydroxyethyl) diphenylethane. Oxidation was carried out in the same manner as the oxidation of 4-bromodiphenylethane. The oxidation products were boiled with ethyl alcohol and filtered. After cooling, benzoic acid crystals came down from the filtrate and had m.p. 119-120°. The oxidation products which were insoluble in ethyl alcohol were fused with phosphorus pentachloride, the cooled fusion was treated with methyl alcohol and poured into a 2-3- fold volume of water. The precipitate which came down was filtered off and recrystallized from aqueous methyl alcohol; m.p. 139-140°. A mixture with the dimethyl ester of terephthalic acid gave no melting point depression.

Ester of 4-(β-hydroxyethyl) diphenylethane and acetic acid. 4 g of 4-(β-hydroxyethyl) diphenylethane, 9 g of acetic anhydride and 0.9 g of freshly fused sodium acetate were heated for 1 hour in a flask under reflux. The reaction mixture was cooled to 40-50°, 90 ml of water was added and it was set aside for 2 hours. It was then extracted several times with ether, the ethereal solution was washed with sodium bicarbonate solution, dried with sodium sulfate, the ether was driven off and the residue was distilled in vacuum, the fraction with b.p. 138-140° (4 mm) was collected. Yield 3 g (64%).

d_{20}^{20} 1.0661, n_D^{20} 1.547, MR_D 80.31; calc. 79.8.

Found %: C 80.52, 80.55; H 7.56, 7.41. $C_{18}H_{20}O_2$. Calculated %: C 80.55; H 7.51.

Ester of 4-(β-hydroxyethyl) diphenylethane and benzoic acid. A suspension was made of 1.5 g 4-(β-hydroxyethyl) diphenylethane in 20 ml 20-30% caustic soda solution in a flask with a ground stopper and to this was added benzoyl chloride in small portions. After the reaction of benzoyl chloride with 4-(β-hydroxyethyl)-diphenylethane had ceased, the reaction product was filtered off and recrystallized from alcohol. Yield 1.6 g (73%), m.p. 91.5-92.5°.

Found %: C 83.16, 83.08; H 6.73, 6.74. $C_{23}H_{22}O_2$. Calculated %: C 83.06; H 6.71.

4-Vinyldiphenylethane. In a Claisen flask with a low soldered outlet was placed 10.2 g 4(β-hydroxyethyl)-diphenylethane, 3.2 g caustic potash and a small amount of hydroquinone. The flask was heated in a bath with Wood's alloy to 220-222° under a residual pressure of 6 mm; the reaction products were condensed in a water condenser. Yield of crude product was 8 g (85%). The crude 4-vinyldiphenylethane was washed 3 times with 10% solution of alkali, then with distilled water until the reaction was neutral, carefully separated from the water, dried with anhydrous magnesium sulfate and vacuum-distilled, the fraction with b.p. 129-131° (4 mm) was collected. The obtained 4-vinyldiphenylethane was repeatedly recrystallized from ethyl alcohol at a temperature of from -18 to -12°. M.p. 29.3-29.7°.

Found %: C 92.30, 92.10; H 7.85, 7.77. M 204,212,206. $C_{16}H_{16}$. Calculated %: C 92 25; H 7.75. M 208.3.

4-(α,β-Dibromoethyl) diphenylethane. 1-2 g 4-vinyldiphenylethane was dissolved in chloroform and a 0.1 N solution of bromine in glacial acetic acid was added at room temperature. The reaction mixture was diluted with water, the solution in chloroform was separated, washed with water, dried and the chloroform was driven off. The solid residue was recrystallized from ethyl alcohol, m.p. 64.5-65.5°.

Polymerization and copolymerization of 4-vinyldiphenylethane. Polymerization and copolymerization were carried out in evacuated sealed ampuls; in all cases benzoyl peroxide was used as the initiator (0.3% of weight of monomers). The temperature rose from 60 to 129° in the course of 90 hours during polymerization of 4-vinyldiphenylethane and its copolymerization with methyl methacrylate. The temperature rose from 60 to 129° in the course of 88 hours during the copolymerization of 4-vinyldiphenylethane with styrene.

SUMMARY

4-Vinyldiphenylethane was synthesized, its polymer and its copolymers with styrene and with methyl methacrylate were obtained, and the high-molecular substances obtained in this manner were characterized.

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SYNTHESIS AND TRANSFORMATIONS OF VINYL ETHERS OF HIGHER POLYATOMIC ALCOHOLS AND CELLULOSE

II. VINYL ETHERS BASED ON CELLULOSE*

M.F. Shostakovsky, E.N. Prilezhaeva and L.V. Tsymbal

In this work we studied the conditions for the extension of the A.E. Favorsky and M.F. Shostakovsky vinylation reaction [1] to cellulose. Interest in the vinyl ethers of cellulose had been shown earlier, but the information existing on them in the literature is extremely contradictory. S.N. Ushakov and I.M. Geller [2] briefly described the preparation of mixed cellulose ethers, containing vinyl and ethyl groups, via the chlorination of ethylcellulose and subsequent cleavage of hydrogen chloride under the influence of either an organic base or alkali. A.E. Favorsky, V.I. Ivanov and Z.I. Kuznetsova [3] indicate the preparation of a mixture of mono-, di- and trisubstituted vinyl ethers of cellulose by treatment of the latter with acetylene in the presence of potassium hydroxide (the exact conditions for running the process are not given). The conclusions as to the composition of the obtained products are based only on elementary analysis. The presence of vinyl groups was shown qualitatively by the liberation of acetaldehyde in acid medium. For the purpose of obtaining vinyl ethers of cellulose V.V. Shtishevsky, A.A. Obolonskaya and N.I. Nikitin [4] treated the latter with acetylene in either water or butanol medium in the presence of 20-40% caustic potash solution at 130-175° for 18-75 hours. The authors assert that instead of vinyl ethers they obtained only difficultly hydrolyzable trimeric acetals.

To realize the direct synthesis of vinyl ethers from cellulose and acetylene, we selected as a model substance, structurally imitating the cellulose unit, the α-methylglucoside molecule. It was shown that the vinylation of the latter is best carried out with a large excess of acetylene in dioxane medium and in the presence of potassium hydroxide [5]. Here "exhaustive" vinylation gave the fully substituted tetravinyl ether of α-methylglucoside in up to 85% yield.

To synthesize the cellulose vinyl ethers, cotton cellulose was first converted into alkali cellulose by treatment with potassium hydroxide,** and then it was heated in dioxane medium with a 10 to 15-fold excess of acetylene against the theoretical required for exhaustive vinylation. The yields of the ethers ranged from 60-80% in which connection the reaction proved to be extremely sensitive to the least disturbance of our found regime. The results of the corresponding experiments are summarized in Table 1. The maximum yield of completely dioxane-soluble ethers with degree of substitution x = 2.0-2.3 is achieved at 130-150° for 5 hours, in which connection further increase in the reaction time fails to lead to a higher degree of substitution, but only to partial decomposition of the molecule. If either a shorter heating time or a lower temperature is employed, then the main reaction product constitutes ethers of comparatively low substitution and proving to be insoluble in dioxane. In a medium of such solvents as, for example, dibutyl ether and dibutyl acetal, being solvents for acetylene and and failing to dissolve the reaction products, the vinylation reaction fails to proceed under these conditions, and instead destruction of the cellulose is observed.

The dioxane-soluble cellulose vinyl ethers were purified by precipitation with water from dioxane and extraction with sulfuric ether.*** After this precipitation an additional portion of ethers (obviously, having a lower molecular weight) was obtained by salting out from the aqueous-dioxane solution with sodium chloride.

*For Communication I see Proc. Acad. Sci. USSR 96, 99 (1954).

**Poorer results were obtained if sodium hydroxide was used for the mercerization.

***The ethyl ether washed out tarry by-products, possessing a disagreeable phenolic odor and showing a higher carbon content than the cellulose vinyl ethers themselves. Judging by the control experiment, similar tars are also formed in the absence of cellulose when acetylene is reacted with alkali in dioxane medium at 130-150° and, apparently, they partially consist of acetylene polymers.

TABLE 1

Synthesis of Cellulose Vinyl Ethers in Dioxane Medium

Reaction conditions		Yield of vinyl ethers (in %)				Yield of ether-soluble tar (in % on the cellulose weight)
Time of heating (in hours)	Temperature of heating	Soluble in dioxane x = 2.0-2.3	Soluble in aqueous-dioxane solution x = 1.3-1.5	Insoluble in dioxane	Total yield	
3	130-150°	13-23	12	25-45 (x = 1.5)	60-70	7-10
5	130-150	46-70	10-12	–	58-80	17-34
11	130-150	58-66	10-12	–	70-77	15-29
17	130-150	53-68	26-29	–	82-84	17-29
5	120-135	8.0	–	44.2 (x = 2.0)	52.2	5-10

As a criterion for the purity of the cellulose ethers we took the agreement of the degree of etherification, calculated from the elementary analysis data, with the value calculated on the basis of titrating the acetaldehyde in the acid hydrolyzate.

The properties of the soluble ethers with a substitution degree of 2.0-2.3 were studied in more detail. They are light, slightly yellowish, infusible, powderlike substances, acquiring the odor of acetaldehyde when stored. They gradually begin to char at 220°. They are readily soluble in pyridine, show limited solubility in dioxane (~ 10%), are even less soluble in chloroform and acetone, show swelling in benzene, xylene and carbon tetrachloride, and are insoluble in water, alcohols, simple ethers, hexane, petroleum ether and cuprammonium solution; their solubility decreases when the operations of solution, precipitation and drying are repeated; evaporation of the solutions fails to yield strong films. The viscosities of the cellulose vinyl ethers in dioxane are shown in Table 2.

TABLE 2

Concentration (in %)	η (relative)
0.1	1.05
1.0	1.77
5.0	17.13

The cellulose vinyl ethers show a number of qualitative reactions, characteristic for other simple vinyl ethers [6]. They decolorize bromine water, and with aqueous acid they give acetaldehyde and a highly destroyed cellulose residue (with a polymerization degree of 40-50). Under the influence of boron etherate in dioxane medium they show slow polymerization, in which connection a 1-2% solution of the vinyl ether congeals to a gel. When shaken with iodine in methanol medium the ethers combine with iodine (75-80% [7], based on x = 2.0).

The degree of etherification shown by the vinyl ethers was determined by titration of the acetaldehyde in the acid hydrolyzate, formed when the weighed ether sample was shaken with 1 N hydrochloric acid at 15-25° (for 10-12 hours).* It is inadvisable to run the hydrolysis at higher temperatures, since at 80° the acetaldehyde is bound as the result of secondary reactions. The experimental results of determining the degree of etherification are summarized in Table 3. For the vinyl ethers, obtained under a vinylation time of 3 to 11 hours, the values of x, determined by the two methods, show good agreement. For the products, obtained as a result of longer heating, even with extremely careful purification such good agreement cannot be achieved, which is evidence that irreversible destructive processes take place here.

As a result, the vinyl ethers, obtained on the basis of cellulose, contain about two vinyl groups per cellulose unit. It is extremely probable that in the first phase the secondary hydroxyl groups on carbon atoms 2 and 3 suffer vinylation, since, as it was recently shown [8], these hydroxyls are considerably more active than are the primary hydroxyl groups of cellulose when the latter is subjected to etherification in alkaline medium.

The course for destruction of the cellulose molecule, proceeding during the synthesis of the vinyl ethers, is shown in Table 4. The greatest damage to the molecule proceeds parallel with the vinylation reaction. Judging by their powderlike nature and the K_ν value of the cellulose residue, formed during their hydrolysis, the degree of polymerization shown by the vinyl ethers should lie in the 40-100 interval [9]. As a result, the vinylation process leads to a roughly 40-fold reduction in the degree of polymerization. At the same time in preparing,

*It was shown by special experiments that crotonization of the acetaldehyde fails to occur under the indicated conditions.

for example, cellulose nitrates, the K_p value is diminished a total of only 5-10 times, and under mild acetylation conditions by only 3-4 times [8]. Consequently, in a strict sense the comparatively low-molecular weight products obtained by us are not "vinyl ethers of cellulose". However, due to the presence of reactive double bonds in them, they can serve as a start for further syntheses based on cellulose.

TABLE 3

Determination of $\underline{x}$ for Dioxane-Soluble Vinyl Ethers of Cellulose, Obtained Under Variable Duration of Vinylation

Expt. Nos.	Duration of vinylation (in hours)	Amount of acetaldehyde (in g per 100 g of substance)		Calculated $\underline{x}$	
		Found by titration after hydrolysis	Calculated from the elementary analysis	From the hydrolysis data	From the elementary composition
25	3	42.6	42.3	2.10	2.05
24	5	42.7	42.3	2.10	2.05
16	11	44.1	44.2	2.20	2.20
17	17	39.3	44.7	1.90	2.30

TABLE 4

Change in the Degree of Polymerization K_p at Different Stages in the Synthesis of Vinyl Ethers

Character of the cellulose	Specific viscosity of an 0.1% cuprammonium solution	K_p
Initial	1.55-1.51	3000-3100
Immediately regenerated from alkali cellulose	0.75-0.95	1500-1900
Regenerated from alkali cellulose, kept under dioxane for 3 days	0.45-0.50	900-1000
Regenerated from alkali cellulose, heated with dioxane for 5 hours at 125-145° in the presence of nitrogen (at 35 atm.)	0.25-0.35	500-700
Formed during the hydrolysis of cellulose vinyl ethers	0.016-0.025	35-50
Regenerated from alkali cellulose, heated in dibutyl ether for 5 hours at 110-130° in the presence of acetylene (pressure 50 atm.)	0.25-0.35	500-700

EXPERIMENTAL

The starting material was refined cotton cellulose which had a moisture content of 5%, ash content 0.5% and degree of polymerization (determined viscosimetrically in 0.1% cuprammonium solution) 3000-3100. The dioxane was purified by the method of Hess and Frahm [10].

Alkali cellulose was prepared directly before the experiment by treatment of pulverized cellulose with a 23% caustic potash solution and subsequent pressing. The total quantity of alkali contained in the alkali cellulose at a pressing coefficient of 3 [11] was about 0.3 g per 1 g cellulose. The alkali cellulose was washed with 50 ml of dioxane to remove excess water. 3-5 g of cellulose was taken for the experiments (10-15 g of alkali cellulose) and 40 ml dioxane per 1 g of cellulose. The experiments were carried out in a rotating autoclave (0.5 liter).

Synthesis of dioxane-soluble vinyl ethers of cellulose. 13.8 g alkaline (potash) cellulose (from 5 g of cellulose), 21.8 g acetylene (32.7 mole per molar cellulose unit) and 200 ml dioxane were taken for the reaction. The acetylene was introduced from a cylinder at room temperature with stirring (under a pressure of 15-17 atm.) until no more of it dissolved in the dioxane. Heating was carried out for 2.5 hours at 130-140° and for 2.5 hours at 140-150°. The maximum pressure in the autoclave was 52 atm. The reaction mixture was a dark-brown almost transparent liquid which was separated by filtration from the residue of resinified alkali and the dioxane was then driven off in vacuum (30-40 mm) until formation of a saturated solution.* The latter was

* When precipitation with water was carried out from dilute dioxane solutions, the vinyl ethers came down in a finely dispersed state, which greatly hindered their subsequent purification.

poured into a 5-fold volume of water for precipitation. The flakes of vinyl cellulose ethers which came down were filtered off through a glass filter, dried in air and extracted with ethyl ether in a Soxhlet apparatus for cold extraction for 3 hours (until the ether that ran down was colorless). After drying in vacuum at 60°, weight 3.8 g.

Found %: C 56.27, 56.20; H 6.57, 6.74; calculated x 2.14.

Found (on hydrolysis) acetaldehyde (in g) per 100 g of substance 42.6, 42.8. Calculated (from data of hydrolysis) %: C 56.4, 56.5; H 6.59, 6.60, x 2a1. Yield 60% on cellulose taken.

After separation of the precipitated vinyl ethers, addition of 5 g of sodium chloride salted out the soluble vinyl cellulose ethers from aqueous-dioxane solution. Weight 0.75 g after washing with water, ethyl ether and drying.

On hydrolysis, found acetaldehyde (in g) per 100 g substance 29.6, 29.4; calculated x 1.44; yield 12% on cellulose taken.

The total yield of vinyl ethers was 72%. After removal of ether from extract obtained by treatment of the vinyl ethers in the Soxhlet apparatus, a dark-colored friable resinous product was obtained with an unpleasant phenolic odor (0.86 g, or 17.2% of weight of cellulose taken).

Found %: C 74.15, 74.03; H 7.86, 7.78.

Synthesis of dioxane-insoluble vinyl ethers of cellulose. a) Heating of 15 g alkaline cellulose (starting from 5 g of cellulose) and 21.8 g acetylene (31.2 moles per molar cellulose unit) in 200 ml dioxane for 3 hours (1.5 hour at 130-140° and 1.5 hours at 140-150°) yielded a dark-brown liquid with a considerable amount of insoluble gelatinous precipitate. By the previously described method, 1.40 g dioxane-soluble ethers was isolated.

Found %: C 56.41, 56.29; H 6.56, 6.50; calculated x 2.10.

Found (after hydrolysis) acetaldehyde per 100 g substance 42.58; calculated x 2.10; yield 23.0%.

Salting out of the aqueous dioxane yielded 0.69 g ethers.

Found acetaldehyde (in g) per 100 g substance 29.5, 29.6; calculated x 1.40; yield 12%.

The dioxane-insoluble residue of vinyl cellulose ethers was washed with water until neutral reaction, dried in air, washed with ethyl ether and dried in vacuum. Weight 1.5 g.

Found acetaldehyde (in g) per 100 g substance 33.57, 33.3; calculated x 1.60; yield 45%.

The total yield of vinyl cellulose ethers was 70%. The quantity of ether-soluble resin was 0.5 g (10% of weight of cellulose).

b) Heating of 15 g alkali cellulose with 21.8 g acetylene in 200 ml dioxane for 5 hours to 110-130° yielded 0.5 g dioxane-soluble vinyl ethers and 3 g dioxane-insoluble ethers which were purified by reprecipitation from pyridine.

Found %: C 56.35, 56.32; H 6.69, 6.69; calculated x 2.10.

Found acetaldehyde (in g) per 100 g of substance 42.1, 41.2; calculated x 2.00; yield 44.2%.

Hydrolysis of vinyl ethers of cellulose in order to determine degree of etherification. A weighed sample of ether (0.15-0.3 g) was placed in a sealed ampul with 10 ml of 1 N hydrochloric acid and shaken on a mechanical shaker for 12 hours (for experiments with heating, the ampul was placed in a water jacket at the required temperature). The ampuls were cooled with ice water, opened, and the contents together with the water-insoluble residue was transferred to 100-ml volumetric flasks. After the solution had cleared, acetaldehyde was titrated by the hydroxylamine method (Table 3). The water-insoluble residue from a number of hydrolysis experiments was washed with water and dried to constant weight. It was a greatly decomposed cellulose.

Found %: C 45.83, 45.79; H 6.58, 6.36. $(C_6H_{10}O_5)_n$. Calculated %: C 44.44; H 6.21.

The residue was soluble in cuprammonium solution, alcohols, acetone and dioxane; it was slightly soluble in ethyl and dibutyl ethers; insoluble in carbon tetrachloride. The degree of polymerization, determined in 0.1% cuprammonium solution, was 40-50.

Reaction of acetylene with KOH in dioxane medium. 2.5 g KOH and 19.5 g acetylene in a medium of 200 ml dioxane were heated in a 0.5-liter autoclave for 5 hours (2.5 hours at 130-140° and 2.5 hours at 140-150°). The reaction mixture was a dark-brown liquid. It was separated from the precipitate of caustic potash and steamed down in vacuum. The resulting dry precipitate was extracted with ethyl ether. After removal of ethyl

ether, from the extract was obtained 1.75 g brown friable resin with a strong phenolic odor.

Found %: C 76.73; H 8.10.

SUMMARY

1. It was shown that vinyl ethers based on cellulose can be synthesized by reacting alkali (potassium) cellulose with acetylene in dioxane medium. Vinyl ethers of highly destroyed cellulose, showing an etherification of 1.3-2.3, were obtained in an overall yield of 65-80%.

2. To determine the degree of etherification shown by the vinyl ethers obtained from cellulose as a base, a method was developed for their quantitative hydrolysis in acid medium.

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TRANSFORMATION AND SYNTHESIS OF CARBOHYDRATES

XIV. STERIC HINDRANCE IN THE AZO-COUPLING OF ARYLGLUCAMINES

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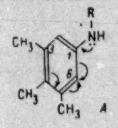
Earlier we had shown [1] that the stereoisomeric 3,4-dimethylphenylglucamines show a dual reactivity in azo-coupling, bound with the stereoisomerism shown by the pentitol substituent on the amino group. Arylglucamines with one unsubstituted position meta to the secondary amino group (the second meta position was occupied by a methyl group) were studied.

It seemed of interest to study in the azo-coupling reaction the behavior of those arylglucamines in which both of the meta positions of the aromatic nucleus are substituted by methyl groups. For 3,4,5-trimethylphenylglucamines both of the ortho positions are equivalent. The reactivity shown by these compounds for azo-coupling in the ortho position is found to depend on the orienting influence shown by the substituents: ortho orientation by the secondary amino group, augmented para orientation by the methyl group in position 3, and ortho orientation by the methyl group in position 5. As a result, the electron density in the ortho position to the secondary amino group, and consequently, the reactivity for azo-coupling shown by compounds with three methyl groups should be greater than for the 3,4-dimethylphenylglucamines, which fail to show supplementary displacement of the electrons bound with the methyl group in position 5 (A).



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Actually, the reverse phenomenon is observed – the reactivity drops; the rate of the azo-coupling reaction reduces to such a degree that at pH 4 the formation, not of trimethylazoglucamines, but only of diazoimino compounds of trimethylphenylglucamines, is observed for all of the stereoisomeric trimethylphenylglucamines. Only at pH below 3 are azo dyes formed, and then only in insignificant yield (see table).

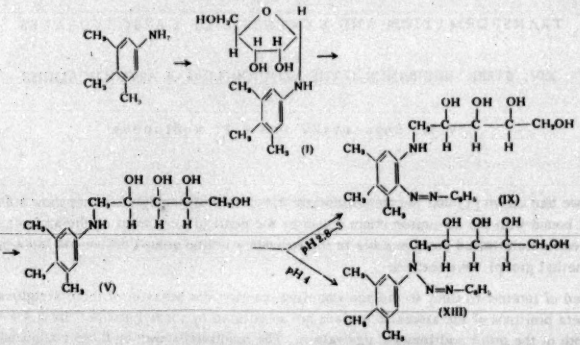
We attribute the reduced reactivity shown by trimethylphenylglucamines for azo-coupling to the presence of steric hindrance factors, produced by the ortho position of the methyl group with respect to the entering azo group. In association with the strong reduction in reactivity shown by glucamines due to steric obstacles, evoked by the methyl group, the influence exerted by the cis, trans hydroxyl groups in the 2' and 3' positions of the pentitol chain on the secondary amino group [1] becomes hardly perceptible on the character of azo-coupling.

The absorption spectra for 3,4-dimethylphenyl-6-phenylazo-d-ribamine and other stereoisomeric azoglucamines show the absorption maxima: λ max. 325 and 471 mμ [1]; the absorption spectra for 3,4,5-trimethylphenyl-6-phenylazo-d-ribamine (IX) and other stereoisomeric azoglucamines (X, XI, XII) are characterized by the absorption: λ max. 333 and 476 mμ. The shifting of the absorption maximum by 12 mμ in the ultraviolet region and by 5 mμ in the visible region is associated with the emergence of substituents from a planar position [2]. As a result, the trimethylphenylazoglucamine molecule that is formed here fails to be a coplanar molecule.

To synthesize 3,4,5-trimethylphenyl-6-phenylazo-d-ribamine (IX) we started from 3,4,5-trimethylaminobenzene and d-ribose, which showed condensation to N-d-ribofuranoside (I); this substance was reduced to the glucamine (V), from which the azo dye (IX) was obtained [2]. The other stereoisomeric azo dyes were obtained in similar manner.

Stereoisomeric N-glucosides were obtained from d-ribose, d-arabinose, d-xylose and d-lyxose with 3,4,5-

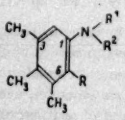
-trimethylaminobenzene in anhydrous alcohol medium under heating. The N-glucofuranosides obtained in this manner show mutarotation; the specific rotation shown by pyridine solutions of the glucosides becomes constant after 48 hours. The N-d-glucofuranosides were obtained in the following anameric forms: 3,4,5-trimethylaminobenzene-N-α-d-ribofuranoside (I); 3,4,5-trimethylaminobenzene-N-α-d-arabinofuranoside (II); 3,4,5-trimethylaminobenzene-N-β-d-xylofuranoside (III) and 3,4,5-trimethylaminobenzene-N-β-d-lyxofuranoside (IV). It should be mentioned that the formation of N-glucosides is associated with the anameric configuration for β-d-arabinose and α-d-xylose-being turned in opposite directions.



The N-glucofuranosides (I, II, III and IV) were converted into stereoisomeric trimethylphenylglucamines (V, VI, VII and VIII) by catalytic hydrogenation with skeletal nickel catalyst. The compounds obtained in this manner were subjected to azo-coupling with phenyldiazonium salts at different pH values, in which connection the stereoisomeric azo dyes (IX, X, XI and XII) were formed at a pH of 2.8-3, while the diazoimino compounds of the stereoisomeric trimethylphenylglucamines (XIII, XIV, XV and XVI) were formed at a pH of 4. The yields of the azo dyes and of the diazoimino compounds, and also their melting points, are summarized in the table.

TABLE

Azo Compounds and Diazoimino Compounds of Stereoisomeric Glucamines



Substance	Substituents			Melting point	Yield (in %) at pH	
	R	R'	R^2		2.8-3.0	4.0
IX	Phenylazo-	d-Ribityl-	H	195-196*	40.3	–
X	"	d-Arabityl-	H	214.5-215	54.7	–
XI	"	d-Xylityl-	H	175-176	83.5	–
XII	"	d-Lyxityl-	H	124-126	46.0	Insignificant
XIII	H	d-Ribityl-	Phenylazo-	158.5*	36.0**	82.0
XIV	H	d-Arabityl-	"	160*	34.5**	99.3
XV	H	d-Xylityl-	"	145*	Small	92.1
XVI	H	d-Lyxityl-	"	145*	37.4**	69.1

* With decomposition

** After addition of sodium acetate to mother liquor.

The structure of the diazoimino compounds of the 3,4,5-trimethylphenylglucamines was determined on the basis of the similarity of their absorption spectra (λ_{max}, 350 mμ) with the absorption spectra of the diazoimino compounds of the 3,4-dimethylphenylglucamines [1], the latter failing to show a second methyl group in the meta position to the secondary amino group.

EXPERIMENTAL

I. N-Glucofuranosides. A mixture of 2 g pentose, 1.8 g 3,4,5-trimethylaminobenzene and 30 ml anhydrous alcohol was heated on a water bath under reflux with shaking until solution was complete (30-40 minutes). Crystallization of the N-glucoside occurred at this point or after cooling or after driving off part of the solvent.

3,4,5-Trimethylaminobenzene-N-α-d-ribofuranoside (I) from d-ribose. Yield 2.28 g (64%) of substance with m.p. 115-116° (with decomp.). After recrystallization from absolute alcohol the product was in the form of colorless needles with m.p. 120-121.5°, $[\alpha]_D$ +164.2° → + 76.8° (2.5% in pyridine).

Found %: N 4.95. $C_{14}H_{21}O_4N$. Calculated %: N 5.24.

3,4,5-Trimethylaminobenzene-N-α-d-arabinofuranoside (II) from d-arabinose. Yield 2.33 g (65.5%) of substance with m.p. 118-119° (with decomp.) in the form of colorless needles (from anhydrous alcohol); $[\alpha]_D$ +75.8° → + 6.3° (5% in pyridine).

Found %: N 5.22. $C_{14}H_{21}O_4N$. Calculated %: N 5.24.

3,4,5-Trimethylaminobenzene-N-β-d-xylofuranoside (III) from d-xylose. Yield 1.65 g (46.5%) of substance with m.p. 118-120° (with decomp.) in the form of colorless needles (from alcohol); $[\alpha]_D^{22}$ -12.6° → -2.6° (5% in pyridine).

Found %: N 5.28. $C_{14}H_{21}O_4N$. Calculated %: N 5.24.

3,4,5-Trimethylaminobenzene-N-β-d-lyxofuranoside (IV) from d-lyxose. Yield 2.6 g (73%) of substance with m.p. 126.5-127° (with decomp.) in the form of colorless needles (from alcohol); $[\alpha]_D$ -117.3° → -45.4° (5% in pyridine).

Found %: N 5.41. $C_{14}H_{21}O_4N$. Calculated %: N 5.24.

II. Glucamines. The above-contained N-glucofuranosides were subjected to hydrolysis with a nickel catalyst at 40-50 atm. and 65-75° for 2-2.5 hours in a rotating autoclave. After the catalyst was separated off, the colorless solution was steamed down in vacuum to low bulk and set aside for crystallization. The precipitate that was obtained was recrystallized from alcohol.

3,4,5-Trimethylphenyl-d-ribamine (V) from N-ribofuranoside (I). From 1.63 g (I) was obtained 0.95 g (58%) methylribamine (V) in the form of lustrous colorless flakes with m.p. 120°; $[\alpha]_D^{21}$ -26.3° (5% in pyridine).

Found %: N 5.42. $C_{14}H_{23}O_4N$. Calculated %: N 5.20.

3,4,5-Trimethylphenyl-d-arabinamine (VI) from d-arabinose. After condensation of arabinose with 3,4,5-trimethylaminobenzene, hydrogenation of the resulting solution yielded the N-glucoside which did not precipitate out. From 2 g arabinose was obtained 2.08 g (58%) methylarabinamine (VI) with m.p. 160.5-161.7° (from alcohol) in the form of colorless elongated prisms; $[\alpha]_D^{25}$ +6.6° (5% in pyridine); $[\alpha]_D^{25}$ + 37.9° (5% in 2 N HCl). The substance gave no melting point depression with the substance prepared by reduction of N-arabinofuranoside (II).

Found %: N 5.27. $C_{14}H_{23}O_4N$. Calculated %: N 5.20.

3,4,5-Trimethylphenyl-d-xylamine (VII) from N-xylofuranoside (III). From 1.65 g (III) was obtained 1.35 g (82%) methylxylamine (VII) in the form of colorless fine needles with m.p. 160-161°; $[\alpha]_D^{22}$ -14.0° (5% in pyridine); $[\alpha]_D^{22}$ -35.9° (5% in 2 N HCl).

Found %: N 4.85. $C_{14}H_{23}O_4N$. Calculated %: N 5.20.

3,4,5-Trimethylphenyl-d-lyxamine (VIII) from N-lyxofuranoside (IV). From 1.52 g (IV) was obtained 1.14 g (76%) methyllyxamine (VIII) in the form of colorless fine needles with m.p. 188-189.5°; $[\alpha]_D^{24}$ +22.1° (5% in pyridine); $[\alpha]_D^{25}$ +35.4° (2.5% in 2 N HCl).

Found %: N 5.40. $C_{14}H_{23}O_4N$. Calculated %: N 5.20.

III. Phenylazo dyes and diazoimino compounds of stereoisomeric glucamines. Carrying out of coupling reactions of methylglucamines with phenyldiazonium sulfate. A solution of 1 g methylglucamine in 100 ml water at 65-80° and 0.5 ml hydrochloric acid was cooled to 20-25° and with stirring was run into a solution of the diazonium salt prepared from 0.46 g aniline, 0.66 g sulfuric acid and 0.34 g sodium nitrite. The azo coupling was carried out at a different pH, which was maintained by careful addition of a 15% sodium acetate solution during the entire course of the reaction. After 2 hours, the precipitate was filtered off and washed with water and dried.

Coupling of phenyldiazonium salt with 3,4,5-trimethylphenyl-d-ribamine (V). 0.56 g (40.3%) azo dye with m.p. 181-183° was obtained at pH 2.8-3. After recrystallization from alcohol, the 3,4,5-trimethylphenyl--6-phenylazo-1-d-ribamine (IX) was obtained in the form of orange-red needles with m.p. 195-196°. The absorption spectrum in ultra-violet and visible light: $\lambda_{max.}$ 246,337,476 mμ (in alcohol).

Found %: N 10.96. $C_{20}H_{27}O_4N_3$. Calculated %: N 11.25.

After addition of sodium acetate, from the mother liquor was obtained 0.5 g (36%) diazoimino compound of methylribamine (XIII) in the form of light-orange needles with m.p. 158.5° (with decomp. from alcohol).

Found %: N 11.10. $C_{20}H_{27}O_4N_3$. Calculated %: N 11.25.

Coupling was at pH 4: yield 1.14 g (82%) diazoimino compound of methylribamine (XIII) with m.p. 158.5° (with decomp. from alcohol).

Coupling of phenyldiazonium salt with 3,4,5-trimethylphenyl-d-arabinamine (VI). At pH 1.8 was obtained 1.05 g (75.5%) of azo dye with m.p. 210°. After recrystallization from alcohol, 3,4,5-trimethylphenyl--6-phenylazo-1-d-arabinamine (X) was obtained in the form of orange-red needles with m.p. 214.5-215°.

Found %: N 11.71. $C_{20}H_{27}O_4N_3$. Calculated %: N 11.25.

Coupling was at pH 2.8-3; yield 0.76 g (54.7%) of azo dye; recrystallization from alcohol yielded 3,4,5--trimethylphenyl-6-phenylazo-1-d-arabinamine (X) with m.p. 214.5-215°.

After azo-coupling and separation of the dye, from the mother liquor, on addition of sodium acetate solution, was obtained 0.48 g (34.5%) of the diazoimino compound of methylarabinamine (XIV) in the form of orange-red needles with m.p. 160° (with decomp. from alcohol).

Found %: N 11.87. $C_{20}H_{27}O_4N_3$. Calculated %: N 11.25.

Coupling was at pH 4; yield 1.38 g (99.3%) of diazoimino compound of methylarabinamine (XIV) with m.p. 160° (with decomp.).

Coupling of phenyldiazonium salt with 3,4,5-trimethylphenyl-d-xylamine (VII). At pH 2.8-3 was obtained 0.82 g (59%) of azo dye; after recrystallization from alcohol, 3,4,5-trimethylphenyl-6-phenylazo-1-d--xylamine (XI) was obtained in the form of orange-red needles with m.p. 175-176°.

Found %: N 11.22. $C_{20}H_{27}O_4N_3$. Calculated %: N 11.25.

After addition of sodium acetate, from the mother liquor was obtained 0.56 g (40.3%) of substance with m.p. 163-166°. After recrystallization from alcohol, an additional 0.34 g (24.5%) of azo dye (XI) was obtained with m.p. 175-176°.

Coupling was at pH 4: yield 1.28 g (92.1%) of diazoimino compound of methylxylamine (XV) in the form of orange-red needles with m.p. 145° (with decomp. from alcohol).

Found %: N 11.66. $C_{20}H_{27}O_4N_3$. Calculated %: N 11.25.

Coupling of phenyldiazonium salt with 3,4,5-trimethylphenyl-d-lyxamine (VIII). 0.64 g (46%) of azo dye with m.p. 115-124° was obtained at pH 2.8-3; after recrystallization from 50% alcohol, 3,4,5-trimethylphenyl-6-phenylazo-1-d-lyxamine (XII) was obtained in the form of orange-red crystals with m.p. 124-126°.

Found %: N 10.81. $C_{20}H_{27}O_4N_3$. Calculated %: N 11.25.

Addition of sodium acetate yielded 0.52 g (37.4%) diazoimino compound of methyllyxamine (XVI) from the mother liquor in the form of yellow needles with m.p. 145° (with decomp. from 50% alcohol).

Found %: N 11.49. $C_{20}H_{27}O_4N_3$. Calculated %: N 11.25.

Coupling was at pH 4: yield 0.96 g (69.1%) diazoimino compound of methyllyxamine (XVI) with m.p. 66-75° (with decomp.), which was in mixture with the azo dye.

SUMMARY

It was shown that stereoisomeric 3,4,5-trimethylphenylglucamines, for which both of the positions meta to the secondary amino group are substituted by methyl groups, suffer steric difficulties when subjected to azo coupling. At pH 2.8-3 azo dyes are formed in insufficient yield, while at pH 4 diazoimino compounds are formed. The absorption spectrum for our obtained sterically hindered azo dyes is shifted toward the long-wave region.

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All-Union Scientific-Research Vitamin Institute

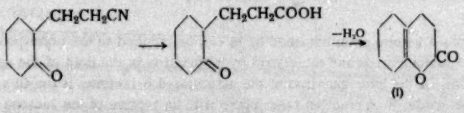
CYANOETHYLATED KETONES IN THE SYNTHESIS OF UNSATURATED δ-LACTONES

V.* THE SYNTHESIS AND PROPERTIES OF UNSATURATED δ-LACTONES FROM MONOCYANOETHYLATED ACETONE AND CYCLOHEXANONE

N.P. Shusherina, R.Ya. Levina and M.Yu. Lurye

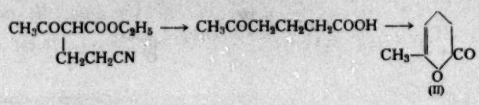
In previous communications we described a new synthesis of unsaturated δ-lactones, using cyanoethylated ketones as starting substances. Thus, from dicyanoethylated cyclohexanone we obtained the unsaturated δ-lactono acid – β(Δ^{8,9}-hexahydro-10-coumaryl)-propionic acid [1], and from monocyanoethylated methyl ethyl ketone – the unsaturated δ-lactone (5,6-dimethyl-3,4-dihydro-α-pyrone) [2].

In the present study we prepared by this method some other members of the slightly studied class of unsaturated δ-lactones: Δ^{9,10}-hexahydrocoumarin (I) and 6-methyl-3,4-dihydro-α-pyrone (II) (from monocyanoethylated cyclohexanone and acetone). Monocyanoethylated cyclohexanone was converted by hydrolysis into 2-cyclohexanone-β-propionic acid, the heating of which with acetic anhydride (and also by simple distillation) gave Δ^{9,10}-hexahydrocoumarin:



(I)

γ-Acetylbutyric acid, the δ-ketono acid corresponding to monocyanoethylated acetone, was obtained by the hydrolysis (with simultaneous decarboxylation) of monocyanoethylated acetoacetic ester [3];** the heating of this acid with acetic anhydride led to the formation of 6-methyl-3,4-dihydro-α-pyrone (II):

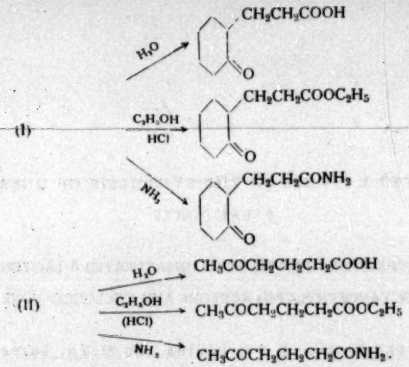


(II)

For the obtained compounds (I and II) the lactone ring was easily opened with either aqueous alkali solution, alcohol (in the presence of hydrogen chloride) or ammonia with the respective formation of the original ketono acids, their esters, or their amides:

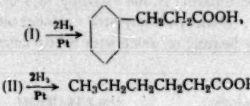
*For Communications III and IV see: Bull. Moscow State University, No. 10, 123 (1955) and Proc. Acad. Sci. USSR, 106, 279 (1956).

**The direct reaction of acrylonitrile with acetone leads to the formation of a mixture of mono- and polycyanoethylated compounds [4].

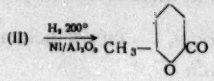


The lactone ring of the unsaturated δ-lactones proved to be resistant to the action of diazomethane, the same as is true for the unsaturated γ-lactones [5].

The catalytic hydrogenation of $\Delta^{9,10}$-hexahydrocoumarin (I) and 6-methyl-3,4-dihydro-α-pyrone (II) was run in the cold over platinum in alcohol solution. Two moles of hydrogen were absorbed per mole of lactone, which led to the formation of saturated acids (β-cyclohexylpropionic and caproic acids, respectively), which were characterized by their crystalline phenylhydrazides:



As a result, the δ ketono acids obtained by us can be reduced to the corresponding saturated acids by a two-stage process – lactonization and subsequent hydrogenation in the cold of the unsaturated δ-lactones in the presence of platinum. If the hydrogenation of the unsaturated δ-lactones is run in a flow system, at 200°, over nickel on aluminum oxide, then reaction takes place without rupture of the lactone ring and leads to the formation of a saturated lactone; thus, from 6-methyl-3,4-dihydro-α-pyrone (II) under these conditions we obtained 6-methyltetrahydro-α-pyrone (similar to the case described by us earlier [2] for 5,6-dimethyl-3,4-dihydro-α-pyrone):



EXPERIMENTAL

Monocyanoethylated cyclohexanone [2-(β-cyanoethyl)-cyclohexanone] was prepared by addition of acrylonitrile (1 mole) to cyclohexanone (5 moles) with stirring at such a rate so that the temperature did not rise above 40°; 40% caustic soda solution in methyl alcohol (2 ml) was used as the catalyst. The obtained nitrile (yield 47%) had constants:

B.p. 146-147° (6 mm), d_4^{20} 1.0215, n_D^{20} 1.4697, MR_D 41.23; calc. 41.19.

Found %: N 9.68, 9.63. $C_9H_{13}ON$. Calculated %: N 9.27.

Literature data: b.p. 147-150° (14 mm) [6]; b.p. 138-142° (10 mm) [7]; b.p. 129-133° (8 mm); n_D^{20} 1.4745, d_4^{20} 1.0181 [8].

2-β-Carboxyethylcyclohexanone (2-cyclohexanone-β-propionic acid). A mixture of 24.5 g nitrile, 40 ml concentrated hydrochloric acid and 20 ml water was boiled for 2 hours. After cooling, the solution was extracted with ether, the ethereal solution was dried with calcium chloride; after driving off the ether, the residue was vacuum-distilled. The obtained acid (yield 24 g, 85.5%) had constants:

B.p. 180-181° (10 mm); m.p. 60-61° (from gasoline), semicarbazone, m.p. 184° (with decomposition, from aqueous alcohol).

Literature data: m.p. 55° [9]; m.p. 62°, semicarbazone, m.p. 194° (with decomp.) [10].

$\Delta^{9,10}$-Hexahydrocoumarin (I).* 10 g cyclohexanonepropionic acid and 18 g acetic anhydride were heated for 4 hours, after which the acetic anhydride was driven off. The obtained $\Delta^{9,10}$-hexahydrocoumarin (yield 7.1 g, 83%) had constants:

B.p. 117-118° at 5 mm, n_D^{20} 1.5050, d_4^{20} 1.1166, MR_D 40.42; calc. 40.54.

Found %: C 70.64, 70.73; H 8.05, 8.02. $C_9H_{12}O_2$. Calculated %: C 71.05; H 7.89.

Hexahydrocoumarin with the same constants was prepared from cyclohexanonepropionic acid by mixing it with acetyl chloride and subsequent vacuum-distillation.

Literature data: b.p. 141-142° (15 mm) [11].

Hydrolysis of hexahydrocoumarin. Under the influence of atmospheric moisture, the lactone partially hydrolyzed, converting to the initial ketono acid. When the lactone was heated with 10% caustic soda solution for 30 minutes, cyclohexanone-2-β-propionic acid formed in quantitative yield; m.p. 59-60° (from gasoline).

Alcoholysis of hexahydrocoumarin. A solution of 5 g lactone in 50 ml anhydrous alcohol was saturated with hydrogen chloride; the reaction mixture was poured in water and extracted with ether. The ethyl ester of cyclohexanonepropionic acid (2-β-carbethoxyethylcyclohexanone) had the following constants:

B.p. 134-135° (7 mm), n_D^{20} 1.4626, d_4^{20} 1.0350, MR_D 52.45; calc. 52.45. According to [10]: b.p. 140-143° (12 mm).

The semicarbazone of the ester (not described previously) had m.p. 105-106° (from aqueous alcohol).

Found %: N 16.55, 16.33. $C_{11}H_{21}O_3N_3$. Calculated %: N 16.47.

The ethyl ester of cyclohexanone-2-β-propionic acid, prepared from the same acid, had the same constants. A mixed sample of semicarbazones melted without depression.

Ammonolysis of hexahydrocoumarin. When hexahydrocoumarin was shaken with aqueous ammonium solution, there immediately came down a white precipitate of the amide of cyclohexanonepropionic acid, which after recrystallization from water, had m.p. 163-164° (with decomp.). According to [10]: m.p. 162-163°.

Catalytic hydrogenation of hexahydrocoumarin (12 g, 0.08 mole) was carried out in the cold over platinum (from PtO_2) in anhydrous alcohol solution; in the course of 3 hours 3.6 liters of hydrogen (0.16 mole) was absorbed. The obtained β-cyclohexylpropionic acid had constants:

B.p. 112-113° (4 mm), n_D^{20} 1.4654, d_4^{20} 1.0104, MR_D 42.76; calc. 42.59.

Literature data: b.p. 143.5° (11 mm), n_D^{20} 1.4634, d_4^{20} 1.0064 [12]; b.p. 112-114° (4 mm), n_D^{20} 1.4596, d_4^{20} 1.0178 [13].

The amide of β-cyclohexylpropionic acid had m.p. 119-120°, the phenylhydrazide had m.p. 155-156° (from aqueous alcohol) (not described in literature).

Found %: N 11.54, 11.74. $C_{15}H_{22}ON_2$. Calculated %: N 11.37.

Two parallel hydrogenation experiments were carried out under the same conditions for hexahydrocoumarin in order to subsequently determine the content of acid in the catalyzate; titration of the hydrogenation products with an alcoholic solution of alkali showed the acid content in them to be 93.5 and 93.8%.

Monocyanoethylated acetoacetic ester. In a flask fitted with stirrer, reflux condenser, thermometer and dropping funnel, was placed 100 ml 95% ethyl alcohol, 0.5 g sodium, 130 g (1 mole) acetoacetic ester and with rapid stirring, 42.2 g (0.8 mole) acrylonitrile was added at such a rate that the temperature did not exceed 40°. The alcohol was then driven off and to the residue, neutralized with acetic acid, ether was added; from the ethereal solution (washed with water and dried with calcium chloride) the ether was driven off. Vacuum-distillation of the reaction product yielded 46 g acetoacetic ester (up to 90° at 20 mm) and 47 g (47%) mono-

*Briefly described previously in Communication III.

cyanoethylated acetoacetic ester with b.p. 165-170° at 20 mm; the residue (25 g) was dicyanoethylated ester with m.p. 82-83° (from alcohol). Monocyanoethylated acetoacetic ester had the following constants:

B.p. 155-156° (10 mm), n_D^{20} 1.4480, d_4^{20} 1.0690, MR_D 45.87; calc. 45.24.

Literature data: b.p. 126-127° (3 mm) [6]; b.p. 143-144° (3 mm), 159-161° (11 mm), n_D^{20} 1.4489, d_4^{20} 1.0682 [14].

γ-Acetylbutyric acid. 30 g monocyanoethylated acetoacetic ester, 17 ml water, 17 ml concentrated sulfuric acid, and 50 ml acetic acid were boiled until evolution of carbon dioxide ceased (5-7 hours). The reaction mixture was diluted with an equal volume of water and extracted with ether in an extractor in the course of 10 hours. Yield 12 g (57%).

B.p. 152-154° (10 mm), n_D^{20} 1.4462, d_4^{20} 1.1100, MR_D 31.54; calc. 31.45. Semicarbazone, m.p. 173° (from aqueous alcohol).

Literature data: b.p. 137-138° (5 mm); semicarbazone, m.p. 173-174° [6].

6-Methyl-3,4-dihydro-α-pyrone (II). 25 g γ-acetylbutyric acid was heated with 100 ml acetic anhydride for 4 hours. Yield 12 g (57%) 6-methyl-3,4-dihydro-α-pyrone.

B.p. 72-73° (10 mm), 82-83° (15 mm), n_D^{20} 1.4650, d_4^{20} 1.0782, MR_D 28.74; calc. 28.89.

When acetyl chloride was used as the dehydrating agent, the yield of lactone increased to 67%.

Literature data: b.p. 194-195° [15], 71-72° (11 mm), n_D^{20} 1.4690 [16].

Hydrolysis of 6-methyl-3,4-dihydro-α-pyrone was carried out by heating it with 10% caustic soda solution; the γ-acetylbutyric acid which formed in quantitative yield was identified by its semicarbazone (m.p. 173°).

Alcoholysis of 6-methyl-3,4-dihydro-α-pyrone was carried out under the same conditions as was the alcoholysis of hexahydrocoumarin. The obtained ethyl ester of γ-acetylbutyric acid had the following constants:

B.p. 104-105° (12 mm), n_D^{20} 1.4275, d_4^{20} 0.9971, MR_D 40.79; calc. 40.80. According to [17]: b.p. 221-222°.

The semicarbazone of the obtained ester had m.p. 114-115°.

Found %: N 19.85, 19.98. $C_9H_{17}O_3N_3$. Calculated %: N 19.38.

Ammonolysis of 6-methyl-3,4-dihydro-α-pyrone yielded the amide of γ-acetylbutyric acid, m.p. 112-113° (from chloroform). According to [18], it had m.p. 114°.

Hydrogenation of 6-methyl-3,4-dihydro-α-pyrone (10 g, 0.089 mole) over platinum (from PtO_2) was carried out in the cold in a solution of anhydrous ethyl alcohol. In the course of 2 hours 2.5 liters of hydrogen was absorbed, corresponding to addition of 2 moles of hydrogen per 1 mole of lactone. After evaporation (in vacuum) of the alcohol, distillation in vacuum yielded caproic acid (7.1 g, 69.7%) with b.p. 105-107° (15 mm), n_D^{20} 1.4190; its phenylhydrazide (not described previously) had m.p. 100° (from aqueous alcohol).

Found %: N 13.82, 13.92. $C_{12}H_{18}ON_2$. Calculated %: N 13.58.

Literature data: b.p. 205° (746 mm) [19], n_D^{15} 1.4188 [20].

Under the same conditions two parallel hydrolysis experiments were carried out on two weighed portions of 6-methyl-3,4-dihydro-α-pyrone; subsequent titration of the hydrogenation products with caustic soda solution gave the following acid content in them: 93.19 and 91.81%.

Hydrogenation of 6-methyl-3,4-dihydro-α-pyrone (15 g) over nickel on aluminum oxide at 180-200° yielded a catalyzate, which after being washed with water and soda, dried with magnesium sulfate and vacuum-distilled (7 g), did not decolorize a solution of bromine in carbon tetrachloride and had no acidic properties. In its constants and analytical data, the obtained hydrogenation product corresponded to the saturated lactone – 6-methyltetrahydro-α-pyrone:

B.p. 114-116° (23 mm), n_D^{20} 1.4425, d_4^{20} 1.0162, MR_D 29.75; calc. 29.36.

Literature data: b.p. 101-102° (11 mm), m.p. 16-18°, n_D^{20} 1.4460 [17].

SUMMARY

1. The cyanoethylation of cyclohexanone, hydrolysis of the resulting nitrile to 2-β-carboxyethylcyclohexanone (2-cyclohexanone-β-propionic acid), and lactonization of the latter led to obtaining (in 83% yield) the

unsaturated δ-lactone – $\Delta^{9,10}$-hexahydrocoumarin.

2. From monocyanoethylated acetone the same series of reactions gave still another unsaturated δ-lactone – 6-methyl-3,4-dihydro-α-pyrone.

3. The structure of the obtained unsaturated δ-lactones was shown by opening their lactone ring and converting them into the original ketono acids, their esters, or their amides.

4. The hydrogenation of unsaturated δ-lactones in the cold over platinum proceeds with the absorption of 2 moles of hydrogen and leads to obtaining the corresponding saturated acids. Lactonization of δ-ketono acids and subsequent hydrogenation of the resulting unsaturated δ-lactones over platinum (in the cold) can be recommended as a method for the reduction of the ketone groups found in the δ-ketono acids obtained by us.

5. Hydrogenation of unsaturated δ-lactones over nickel on aluminum oxide, at 180-200°, leads to the formation of the corresponding saturated δ-lactones.

6. Some new crystalline derivatives of γ-acetylbutyric, cyclohexanonepropionic, β-cyclohexylpropionic and caproic acids were described.

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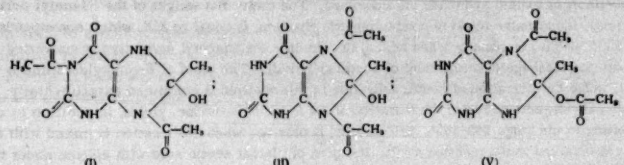
*T.p. = C.B. Translation pagination

STRUCTURE OF THE TRIACETYL DERIVATIVE OF 4,5-DIAMINOURACIL

V.I. Khmelevsky and O.I. Durnitsyna

Uric acid under prolonged heating in acetic anhydride is converted into 8-methylxanthine. This reaction, extensively used for the commercial preparation of 8-methylxanthine, proceeds with the formation of a number of intermediate compounds, one of which is the triacetyl derivative of 4,5-diaminouracil, having the empirical formula $C_{16}H_{18}O_8N_4$.

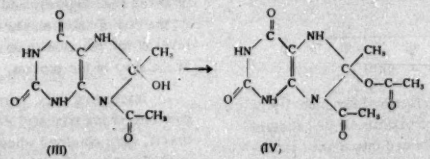
The triacetyl derivative of 4,5-diaminouracil was first prepared by the acetylation of 4,5-di-(acetylamino)-uracil (VII) with acetic anhydride, and also by heating uric acid with acetic anhydride in the presence of pyridine [1]. Biltz and Schmidt [2] isolated the indicated triacetyl derivative when they heated the sodium salt of 4,5-diaminouracil with acetic anhydride. They considered the compound to be the diacetyl derivative of 2,6-dioxo-8-hydroxy-8-methylhexahydropurine, in which one of the acetyl groups is found at N^9,



(I) (II) (V)

and the second group at either N^1 (I) or at N^7 (II). Biltz and Schmidt failed to attribute any special significance to the triacetyl derivative of 4,5-diaminouracil and regarded it as a secondary reaction product.

The opinion that the triacetyl derivative of 4,5-diaminouracil is an intermediate compound in the synthesis of 8-methylxanthine from uric acid was first expressed by Strukov and Diskina [3]. These investigators believed that the triacetyl derivative of 4,5-diaminouracil (IV) is formed in the process of transforming uric acid into 8-methylxanthine via acetylation of the diacetyl derivative of 4,5-diaminouracil (III):



(III) (IV)

In accord with the representation of Biltz and Schmidt, Strukov and Diskina depicted the diacetyl derivative of 4,5-diaminouracil (III) as being 2,6-dioxo-9-acetyl-8-hydroxy-8-methylhexahydropurine, and the triacetyl derivative (IV) as being 2,6-dioxo-9-acetyl-8-acetoxy-8-methylhexahydropurine.

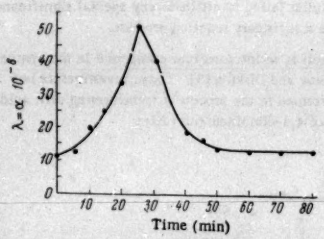
In 1953 Bredereck, Hennig and Pfleiderer [4] experimentally confirmed the validity of the postulation made by Strukov and Diskina. They showed that the triacetyl derivative of 4,5-diaminouracil is actually an intermediate product in the transformation of uric acid into 8-methylxanthine, and improved the method of its

direct preparation from uric acid. Contrary to Strukov and Diskina, Bredereck and coworkers regarded the triacetyl derivative of 4,5-diaminouracil as being 2,6-dioxo-7-acetyl-8-acetoxy-8-methylhexahydropurine (V).

On the basis of the investigations that were made it was considered established that the triacetyl derivative of 4,5-diaminouracil is the diacetyl derivative of 2,6-dioxo-8-hydroxy-8-methylhexahydropurine and, consequently, shows a bicyclic structure. The opinions of the various investigators differed only in respect to the position of one acetyl group. Such a viewpoint relative to the structure of the triacetyl derivative permits explaining only its transformation into 8-methylxanthine. The other chemical properties of this compound do not support its bicyclic structure.

Thus, for example, when dissolved in hot water the triacetyl derivative of 4,5-diaminouracil is quite rapidly transformed into the diacetyl derivative, which is, as has been firmly established at the present time [5], 4,5-di-(acetylamino)-uracil (VII). The formation of the latter cannot be explained with the aid of the structural formulas (I, IV and V) proposed for the triacetyl derivative of 4,5-diaminouracil.

In connection with this we ran some experiments to study further the chemical properties and structure of the triacetyl derivative of 4,5-diaminouracil. We obtained this compound by boiling uric acid in a mixture of pyridine as solvent and acetic anhydride. The technical product was purified via rapid crystallization from 30 volumes of water. The triacetyl derivative shows low stability in hot water and is hydrolyzed to 4,5-di-(acetylamino)-uracil (VII). Judging from the appearance of acetic acid odor, the hydrolysis already proceeds at the moment of solution. During the hydrolysis process one acetyl group is removed to give acetic acid and a molecule of 4,5-di-(acetylamino)-uracil (VII). Three equivalents of sodium hydroxide are consumed in the conductometric titration* of the water-recrystallized triacetyl derivative of 4,5-diaminouracil and 3 distinct titration areas are formed. In contrast to the triacetyl derivative, only two titration areas are formed in the conductometric titration of 4,5-di-(acetylamino)-uracil (VII) under similar conditions and, correspondingly, only 2 equivalents of sodium hydroxide are consumed. The molecular weight of the triacetyl derivative of 4,5-diaminouracil, found as the result of conductometric titration, is equal to 268, which corresponds to the empirical formula of this compound. When heated in quinoline the triacetyl derivative is converted into 8-methylxanthine with the cleavage of a molecule of acetic anhydride. The yield of 8-methylxanthine is close to the theoretical, while the liberation of acetic anhydride in this reaction is confirmed experimentally. Distillation of the mother liquor, obtained from the filtration of the 8-methylxanthine, yields, in addition to quinoline, a fraction boiling in the range 140-165°. Self-heating is observed when this fraction is mixed with aniline, and acetanilide is obtained as the reaction result. Reaction of glacial acetic acid with aniline under these conditions fails to yield acetanilide.



Data on the change in electrical conductivity of the medium when 4-acetylamino-5-di-(acetylamino)-uracil is transformed into 8-methylxanthine.

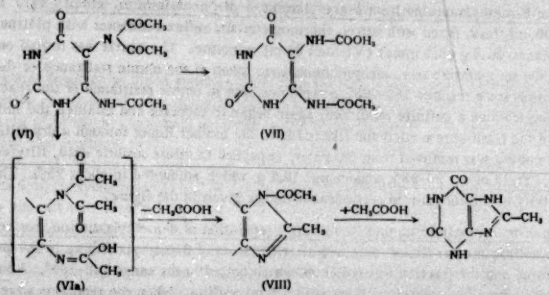
The transformation of the triacetyl derivative into 8-methylxanthine is accompanied by a peculiar change in the electrical conductivity of the reaction mass. This change during the reaction process can be observed by measuring the ohmic resistance of the reaction medium with the aid of a conductometer. At the start a sharp rise in electrical conductivity is observed (see figure), and then a similar sharp drop. At the end of reaction the electrical conductivity level of the reaction mass remains nearly the same as at the start of the process.

Interesting data, permitting us to judge as to the structure of the triacetyl derivative of 4,5-diaminouracil, were obtained when we treated this compound with glacial acetic acid. The boiling of the triacetyl derivative in 100% acetic acid, the same as when it is heated in water, yields 4,5-di-(acetylamino)-uracil (VII). Such a transformation of the triacetyl derivative under the influence of acetic acid cannot be explained by any of the proposed structural formulas (I, IV, V). Judging from literature data [6], a similar acidolysis of one acetyl group can be observed for diacetanilide, the boiling of which in acetic acid results in the cleavage of one acetyl group and the formation of acetanilide. A

*The conductometric titration of the obtained substances was made by V.F. Degtyarev.

similar behavior shown by the triacetyl derivative of 4,5-diaminouracil under these conditions permitted us to conclude that of the three acetyl groups, two are attached to one nitrogen atom, the same as holds true for diacetanilide. When it is considered that the triacetyl derivative can be obtained from 4,5-di-(acetylamino)-uracil (VII), the ability of this compound to be transformed into 8-methylxanthine, and also the peculiarities shown in the chemical properties of the individual amino groups, it can be concluded that the two acetyl groups are attached to N^5. With such an arrangement of two of the acetyl groups, the triacetyl derivative of 4,5-diaminouracil can only be 4-acetylamino-5-di-(acetylamino)-uracil (VI).

Such a representation of the structure of the triacetyl derivative of 4,5-diaminouracil shows good agreement with its chemical properties. Thus, for example, the formation of 4,5-di-(acetylamino)-uracil (VII) becomes understandable when this compound is reacted with acetic acid:



The formation of 8-methylxanthine from 4-acetylamino-5-di-(acetylamino)-uracil (VI) is possible only via preliminary cleavage of acetic acid and subsequent acidolysis of the resulting intermediate product (VIII). This scheme is found in full accord with the data on the change in the electrical conductivity of the medium when the triacetyl derivative of 4,5-diaminouracil is transformed into 8-methylxanthine (see figure).

EXPERIMENTAL

Preparation of 4-acetylamino-5-di-(acetylamino)-uracil (VI). In a 1000 ml round-bottomed flask fitted with reflux condenser, fastened on a ground end, was placed 106 g 95% commercial uric acid, 300 ml acetic anhydride and 100 ml pyridine-solvent (b.p. 125-135°) or pyridine. The obtained mixture was boiled for 5-5.5 hours until evolution of carbon dioxide ceased. To avoid scorching of the uric acid, the contents of the flask had to be shaken vigorously until boiling started. After the evolution of carbon dioxide ceased, the reaction mass was cooled to room temperature, filtered and the precipitate on the filter was carefully washed with dry dichloroethane and absolute ether. Yield of dry commercial 4-acetylamino-5-di-(acetylamino)-uracil was 133 g, which amounted to 83.5%, calculated on uric acid taken for reaction.

Purification of the obtained triacetyl derivative of 4,5-diaminouracil was carried out in portions by rapid crystallization from a 30-fold quantity of water. The precipitate on the filter was washed with a small quantity of ethyl alcohol and then with ether. The total yield of pure substance was 65-66 g.

Results of conductometric titration: 0.2132 g subst.: 2.4 ml N NaOH. Found 0.2136 g subst.

Formation of acetic acid on hydrolysis of 4-acetylamino-5-di-(acetylamino)-uracil (VI) with water. 6.7 g (0.025 mole) 4-acetylamino-5-di-(acetylamino)-uracil, recrystallized from water, was placed in a round-bottomed flask and treated with live steam for 2 hours. About 930 ml of distillate was carefully collected and the acetic acid content was determined by conductometric titration. Analysis showed the distillate to contain 1.2 g (80%) acetic acid.

Preparation of 4,5-di-(acetylamino)-uracil (VII) from 4-acetylamino-5-di-(acetylamino)-uracil (VI). a) Hydrolysis with water. 20 g of commercial product (VI) was boiled in 600 ml water for 30 minutes and filtered free of insoluble 8-methylxanthine precipitate. The filtrate was purified with a small amount of charcoal and steamed to dryness. Yield of dry 4,5-di-(acetylamino)-uracil was 14.4 g (85.7%). The weight of filtered 8-methylxanthine was 2.8 g.

Results of conductometric titration: 0.2095 g subst.: 1.85 ml N NaOH. Found 0.2090 g subst.

b) Acidolysis of acetic acid. In a 100 ml flask fitted with reflux condenser, fastened on a ground end, was placed 5 g of dry substance (VI), recrystallized from water, and 50 ml of 100% acetic acid. The contents of the flask were heated to the boil. After about 18-20 minutes, all the triacetyl derivative taken for reaction went into solution and within a small interval of time a precipitate of 4,5-di-(acetylamino)-uracil started to come down. Acidolysis of the triacetyl derivative was completed on boiling the contents of the flask for an hour. The precipitate which came down was filtered off, washed from acetic acid with dry dichloroethane, absolute ether and dried in a vacuum-desiccator over caustic soda. The weight of the obtained substance (VII) was 3.4 g (81%).

Results of conductometric titration: 0.1366 g subst.: 1.20 ml N NaOH. Found 0.1356 g subst.

Preparation of 8-methylxanthine from 4-acetylamino-5-di-(acetylamino)-uracil (VI). In a 3-necked round-bottomed 200 ml flask, fitted with stirrer, thermometer and reflux condenser with platinum electrodes fixed inside, was placed 26.8 g (0.1 mole) (VI) and 80 ml quinoline. The heater was turned on and with continuous stirring, as the temperature rose, measurements were taken of the ohmic resistance of the contents of the flask. After the temperature reached 160-165°, a rapid decrease in ohmic resistance of the reaction mass was noted, which, having reached a definite minimum, again began to increase and attained the initial level. After this, the contents of the flask were cooled and filtered from the mother liquor through a dry filter. The precipitate of 8-methylxanthine was removed from the filter, suspended in dilute sulfuric acid, filtered and carefully washed with water. Yield of dry 96-98% product was 16.3 g, which amounted to about 95%. The data on the change in conductivity of the medium in reciprocal ohms are given in the figure.

Investigation of the quinolinic mother liquor, after separation of 8-methylxanthine, for acetic anhydride content. 40 ml quinolinic mother liquor, obtained after filtration of 8-methylxanthine in the preceding experiment, was fractionated and the fraction was collected which boiled in the range 140-165°. About 4 ml of the fraction obtained was mixed (ice-water cooling) with 3.5 ml aniline. When the reactants were combined, it was observed that the temperature rose to 70°. The mixture was cooled to room temperature and set aside in a closed flask for 12 hours. The crystalline precipitate of acetanilide which came down was filtered off, washed with cold water and dried. Yield of dry acetanilide with m.p. 114-115° was 2.2 g.

SUMMARY

1. The chemical properties of the triacetyl derivative of 4,5-diaminouracil were studied.

2. It was shown that the given compound is 4-acetylamino-5-di-(acetylamino)-uracil (VI).

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SYNTHESIS AND STUDY OF 2-PHENYL-1,3-INDANDIONE

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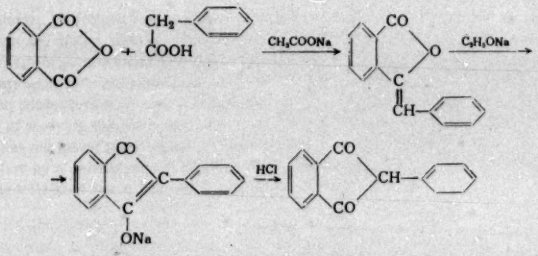
Substances that function as blood anticoagulants find themselves the center of medical attention; in some illnesses coagulation of the blood takes place inside of undamaged vessels, which leads to the formation of clots (thrombi), capable of blocking the vessels necessary for metabolic activity [1]. At the present time a whole series of biological and synthetic preparations, functioning as blood anticoagulants, is known, for example heparin, hirudin, dicoumarol, Tromexan, Marcoumar, etc. [2]. In general the last three show a close structure and are derivatives of 4-hydroxycoumarin [3]. The fundamental disadvantage of all of these compounds is the fact that their action appears only after a long time (1 to 3 days) and lasts up to 10 days. In addition, dicoumarol is characterized by high toxicity and in the case of overdosage produces pain in the spine and other organs, which caused it to be classified as a poison [4]. Tromexan shows its effectiveness when used in large doses and its use proves to be cumulative in the organism. Marcoumar is less toxic than dicoumarol, but its synthesis is characterized by some complexity. In 1954 [5] a new derivative of 4-hydroxycourmarin was described, 3,3'--furfurylidenebis(4-hydroxycoumarin), which is nontoxic, proves effective in 48 hours and when used on rabbits it eliminates the condition associated with blood-vessel thrombosis in 4-6 days.

In connection with the above, we turned our attention to 2-phenyl-1,3-indandione, first described by Gabriel [6]. We synthesized this compound by condensing phthalic anhydride with phenylacetic acid in the presence of sodium acetate, with subsequent isomerization of the resulting benzalphthalide (in the presence of sodium ethylate), resulting in that, due to rupture of the lactone grouping and enol formation at the carbon in the 3 position, the phenylcarbon radical suffers migration, which on acidification leads to 2-phenyl-1,3-indandione:



Pharmacological testing of the preparation synthesized by us, made by R.Ya. Polyak under the supervision of V.V. Zakusova, revealed that the preparation is completely nontoxic, and for rabbits, in contrast to known preparations, it shows considerably faster action (within 10-12 hours), in which connection it fails to exhibit any secondary effect.

EXPERIMENTAL

Benzalphthalide. 110 g phthalic anhydride, 100 g phenylacetic acid and 2.5 g anhydrous sodium acetate

were heated for 2 hours with concurrent driving off of water. The obtained benzalphthalide was extracted with hot alcohol (800 ml); yield 128 g (78%) with m.p. 96-98°.

2-Phenyl-1,3-indandione. 22 g benzalphthalide was dissolved with heating in 150 ml anhydrous alcohol and to the solution was added 50 ml 6% sodium ethylate solution and the yellowish solution became dark red. After alcohol was driven off, acicular red crystals separated out which were dissolved in water and acidified with hydrochloric acid. Yield 22 g (100%) of substance with m.p. 145°.

Found %: C 81.01, 80.99; H 4.53, 4.53. M 217.2, 227.8. $C_{15}H_{10}O_2$. Calculated %: C 81.15; H 4.53. M 222.0.

2-Phenyl-1,3-indandione was readily soluble in alcohol and in ether, giving an orange coloration, and in solutions of alkali hydroxides and carbonates – a red coloration. The action of acids decolorized the alkaline solutions.

SUMMARY

2-Phenyl-1,3-indandione was synthesized from phthalic anhydride and phenylacetic acid, followed by isomerization of sodium derivative of the resulting benzalphthalide, and its properties were described.

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REDUCTIVE PROPERTIES OF α-NAPHTHYLMETHYLMAGNESIUM CHLORIDE IN SOME GRIGNARD REACTIONS

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In order to synthesize tertiary carbinols with α-naphthylmethyl radicals we proceeded from α-naphthylmethylmagnesium chloride and aryl ketones; in addition to tertiary alcohols, it was assumed here that dehydration products could also be formed, but, as the experimental data revealed, when acetophenone, benzophenone, phenyl α-naphthyl ketone or di-α-naphthyl ketone were used as the ketones, reductive reactions predominated in nearly all cases, and the ketones behaved as though they were nonparticipants in these reactions. Thus, for example, the reaction of α-naphthylmethylmagnesium chloride with either acetophenone or benzophenone gave α-methylnaphthalene and di-α-naphthylethane. When the reaction was run with benzophenone and the reaction conditions were changed in that the reaction of α-naphthylmethylmagnesium chloride with the ketone was run in a nitrogen stream, a substance was obtained which when brominated led to a monobromo derivative having the composition $C_{24}H_{17}Br$. Here it could be assumed that the first-formed 1,1-diphenyl-2-α-naphthylmethylcarbinol suffered dehydration, and the resulting 1,1-diphenyl-2-α-naphthylethylene then underwent bromination:

$$(C_6H_5)_2COH-CH_2-C_{10}H_7\text{-}\alpha \xrightarrow{-H_2O} (C_6H_5)_2C=CH-C_{10}H_7\text{-}\alpha \xrightarrow{Br_2}$$
$$(C_6H_5)_2CBr-CHBr-C_{10}H_7\text{-}\alpha \xrightarrow{-HBr} (C_6H_5)_2C=CBr-C_{10}H_7\text{-}\alpha.$$

The reaction of α-naphthylmethylmagnesium chloride with either phenyl α-naphthyl ketone or di-α-naphthyl ketone gave di-α-naphthylethane and α-methylnaphthalene.

Consequently, as follows from the presented data, independent of the nature of the ketones the same reduction products are always formed. The di-α-naphthylethane and α-methylnaphthalene were identified as their picrates with m.p. 105.5 and 139-141°, respectively. In this connection the starting ketones were recovered in amounts up to 80% and more, and also showed partial tarring. It is possible that the tars represented polymerization products of unsaturated compounds, formed in the dehydration of the tertiary alcohols; with the exception of studying the reaction product from benzophenone and α-naphthylmethylmagnesium chloride, this problem was not investigated closer. If the formation of di-α-naphthylethane in a number of syntheses can be explained by a pairing of radicals, then evidently the formation of α-methylnaphthalene proceeds as the result of hydrolysis of the α-naphthylmethylmagnesium chloride.

EXPERIMENTAL

Reaction of α-naphthylmethylmagnesium chloride with acetophenone. To 2.4 g magnesium in 100 ml ether was gradually added 17.8 g α-chloromethylnaphthalene in 50 ml ether and then 8 g acetophenone in 50 ml ether was added with stirring to the resulting organomagnesium compound. After being heated for 3 hours on a water bath with reflux, the mixture was set aside overnight and decomposed with a saturated aqueous solution of ammonium chloride with ice. The ethereal solution was dried over calcined sodium sulfate. After the ether was driven off, a viscous mass was obtained from which fine white crystals soon started to separate out. After separation, washing with ether, and recrystallization from alcoholic-benzene mixture (1:1), 4.8 g di-α-naphthylethane was obtained with m.p. 160-161°, which amounted to 34% with respect to α-chloromethylnaphthalene (literature data give m.p. 160° [1]).

The picrate of di-α-naphthylethane was prepared for identification. 0.24 g of substance with m.p. 160-161° in 5 ml benzene was mixed with 0.42 g picric acid in 5 ml benzene and after boiling, the separated crystals were filtered off and recrystallized from an alcoholic-benzene mixture (1:1). M.p. 105.5° (literature data give m.p. 105° [1]).

Upon investigation of the filtrate after separation of di-α-naphthylethane, 6.5 g of substance was obtained with b.p. 200-210° (acetophenone), 2.1 g of substance with the odor of acetophenone with b.p. 218-242° and 9.5 g dark-brown viscous resin. Fraction 200-210° boiled at 201-205° after a second distillation; its 2,4-dinitrophenylhydrazone had m.p. 273° and gave no depression in a mixed sample with known 2,4-dinitrophenylhydrazone of acetophenone [2]. A second distillation of fraction 218-242° yielded a substance with b.p. 237-240°; the picrate which was prepared from it had m.p. 139-141° (the literature data give the picrate of α-methylnaphthalene m.p. 141° [3]). A mixed sample with the picrate of α-methylnaphthalene gave no depression.

The data of four experiments showed that more than 80% of the acetophenone did not react; the average yield of α-methylnaphthalene was about 20%, that of di-α-naphthylethane – about 36%.

Reaction of α-naphthylmethylmagnesium chloride with benzophenone. To the organomagnesium compound, prepared from 2.4 g magnesium and 17.6 g α-chloromethylnaphthalene in 100 ml ether was gradually added 18.2 g benzophenone in 100 ml ether with stirring. The reaction was carried out in a nitrogen atmosphere. The reaction mixture was heated for 3 hours on a water bath and the next day it was decomposed with saturated aqueous solution of ammonium chloride with ice. After the larger portion of the ether was driven off, fine white crystals separated out, which after separation and recrystallization from alcohol-benzene mixture (1:1) had m.p. 161-162° and gave no depression with di-α-naphthylethane. Yield 2.8 g (~20% on α-chloromethylnaphthalene). After separation of di-α-naphthalene, the residue was a viscous yellow non-crystallizing resinous substance, which was distilled; this yielded 2.4 g substance, b.p. 127-135° at 6 mm; 5.1 g substance, b.p. 134-137° at 7 mm and ~20 g dark-brown viscous resinous mass. After re-distillation, fraction 127-135° boiled at 199.5-203°, and its picrate, similar to the previously described one, had m.p. 139-141° and gave no depression with known picrate of α-methylnaphthalene. Fraction 137-147° at 6 mm crystallized; after recrystallization from alcohol, it had m.p. 47-48° and gave a 2,4-dinitrophenylhydrazone with m.p. 237.5-238°. A mixed sample with known 2,4-dinitrophenylhydrazone of benzophenone [4] gave no depression.

To 13.5 g of resinous residue, which remained after separation of benzophenone and dissolved in 50 ml of 80% acetic acid, was added drop-wise with vigorous stirring and cooling to -2 to +6° a solution of 6.4 g of bromine in 25 ml 80% acetic acid. The reaction mixture was poured in water; a yellow flocculent precipitate separated out, which after repeated washings with water and treatment with steam, converted to a viscous dark-brown resinous mass. After solution in ether, drying over calcined sodium sulfate and driving off the ether, the residue was dissolved in hot alcohol; lustrous crystals separated out which were slightly yellowish. After a second crystallization from alcohol, 0.85 g of substance was obtained with m.p. 124-126°.

Found %: Br 20.75. $C_{24}H_{17}Br$. Calculated %: Br 20.73.

5.8 g bromide, 10 ml ethyl ether, 397 ml 1% potassium permanganate solution and 3 g soda were shaken for 6 hours and then the reaction mixture was set aside overnight. The colorless solution was separated from the manganese dioxide and after washing the latter with hot water and drying, it was extracted with hot alcohol. On cooling, a white precipitate separated out from alcoholic solution, which after recrystallization from alcohol, had m.p. 48-49° and gave no depression in mixed sample with benzophenone.

After separation of the manganese dioxide, the aqueous filtrate was concentrated to low bulk, neutralized with nitric acid (in presence of phenolphthalein) and after boiling, was filtered into a 100 ml volumetric flask. After diluting with water up to the mark in aliquot parts of the given solution, potassium bromide was determined (Vohlhard) and potassium naphthonate was titrated with 0.1 N hydrochloric acid solution in presence of 25 ml ether and methyl orange indicator.

a) On 25 ml of solution, used for quantitative determination of naphthoic acid, 37.0 ml 0.1 N HCl solution was spent; b) on another 25 ml of solution, used for determination of bromide, 37.0 ml 0.1 N $AgNO_3$ solution was spent. Found g: $C_{10}H_7COOH$ 0.6360; KBr 0.4403. Calculated for $C_{10}H_7COOH$ in given volume 0.6478 g, KBr 0.4480 g.

The action of the above-mentioned neutralized solution of hydrochloric acid yielded a white precipitate, which after recrystallization from alcohol, had m.p. 160-161° and was α-naphthoic acid [5].

Found %: C 76.64, 76.46; H 4.66, 4.68. $C_{11}H_8O_2$. Calculated %: C 76.74; H 4.65.

On the basis of the analytical data on the formation, upon oxidation, of benzophenone, naphthoic acid and potassium bromide, it follows that the substance has the structure of 1,1-diphenyl-2-bromo-2-α-naphthylethylene.

Reaction of α-naphthylmethylmagnesium chloride with phenyl α-naphthyl ketone. To 2.4 g magnesium in 75 ml ether was added with stirring a solution of 18 g α-chloromethylnaphthalene in 50 ml ether. After heating for 2 hours to the boiling point of ether and subsequent cooling at 15-20°, a solution of 15 g phenyl α-naphthyl ketone in 75 ml ether was gradually added to the reaction mixture. Then, after 2 hours of heating on a water bath, the reaction mixture, upon cooling, was decomposed with an aqueous solution of ammonium chloride with ice. The ethereal solution was dried and approximately 60-70% ether (by volume) was driven off; 4.7 g of substance separated out, which after recrystallization from alcohol-ether mixture (1:1) had m.p. 160-161° and gave no depression in a mixed sample with known di-α-naphthylethane. Yield 33.5% with respect to α-chloromethylnaphthalene. After separation of di-α-naphthylethane, the residue was a viscous, resinous, yellow substance. Distillation of 20 g of the latter yielded 5.2 g colorless, oily liquid with b.p. 125-135° at 7 mm and 12.7 g of bright-yellow viscous mass with b.p. 212-220° at 7 mm, which almost immediately crystallized. After a second distillation, the 1st fraction had b.p. 240-245° (at normal pressure). The picrate, prepared by reacting the benzene solutions of the substance with picric acid, had m.p. 139-142° after recrystallization from alcohol and gave no depression in a mixed sample with the picrate of α-methylnaphthalene; yield 6.5% with respect to α-chloromethylnaphthalene. The crystals, obtained from the second fraction, had m.p. 74-75° after recrystallization from alcohol and gave no depression in a mixed sample with known phenyl α-naphthyl ketone. After distillation, the residue (about 8 g) was a dark-brown viscous resin which was not investigated in more detail.

Reaction of α-naphthylmethylmagnesium chloride with di-α-naphthyl ketone. To the α-naphthylmethylmagnesium chloride, prepared the same as before from 2.4 g magnesium, 17.6 g α-chloromethylnaphthalene and ether, was added gradually with stirring a solution of 10 g di-α-naphthyl ketone in 200 ml ether. After heating on a water bath for 2 hours and decomposing with a solution of ammonium chloride with ice 12 hours later, the ethereal layer was separated, dried and after driving off the greater part of the ether, 5.1 g of crystalline substance separated out, which after recrystallization from an alcohol-benzene mixture (1:1), had m.p. 161-162° and gave no depression in a mixed sample with known di-α-naphthylethane. Yield 36.1% with respect to α-chloromethylnaphthalene. From the yellow resinous residue, after separation of di-α-naphthylethane, coarse white crystals separated out after several days, which were separated from the resin by addition of acetic anhydride, in which the resin dissolved. Isolated 6 g of crystalline substance, which after recrystallization from acetic anhydride, had m.p. 97.5-99°. Mixed samples with known di-α-naphthyl ketone and its 2,4-dinitrophenylhydrazone with m.p. 269-270° gave no depression. As the obtained data show, 60% of the di-β-naphthyl ketone did not react with magnesiumchloro-α-methylnaphthalene.

20 g of resinous substance was distilled; 5.8 g colorless oily liquid with b.p. 120-137° at 7 mm was obtained, from which a picrate was prepared that had m.p. 140.5-142° and gave no depression in a mixed sample with previously prepared picrate of α-methylnaphthalene.

SUMMARY

1. The reaction of α-naphthylmethylmagnesium chloride with acetophenone, benzophenone, phenyl α-naphthyl ketone and di-α-naphthyl ketone was studied; here it was found that in nearly all cases pairing of the α-naphthylmethylene radicals occurs with the formation of di-α-naphthylethane; in addition, α-methylnaphthalene is formed.

2. The reaction of α-naphthylmethylmagnesium chloride with benzophenone was studied in a stream of nitrogen; here it was found that, in addition to di-α-naphthylethane and α-methylnaphthalene, 1,1-diphenyl-2-α-naphthylethylene is formed. The presence of the latter was shown by bromination and oxidation of the bromide.

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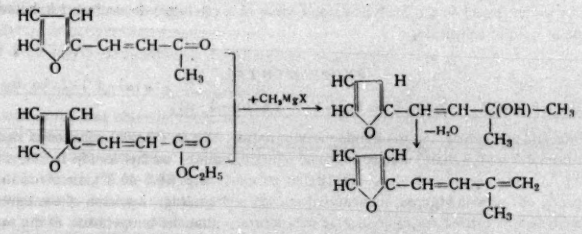
THE PREPARATION AND SOME PROPERTIES OF 1-(2-FURYL)-3-METHYL-1-BUTEN-3-OL

A.A. Arsenyuk

In our previous studies we had presented experimental data on the preparation and study of some of the properties of 1-(2-furyl)-1-propen-3-ol, 1-(2-furyl)-3-alkyl-1-propen-3-ols, and their acetates [1,2]. The present investigation is devoted to the organomagnesium synthesis of 1-(2-furyl)-3-methyl-1-buten-3-ol from furfurylideneacetone, and also from the ethyl ester of β-(2-furyl)-acrylic acid. This alcohol shows interest as a possible starting substance for the synthesis of 1-(2-furyl)-3-methyl-1,3-butadiene.



The reaction of organomagnesium compounds with α,β-unsaturated ketones of the furan series, containing a conjugated system of double bonds, has been studied by a number of investigators [3-6]. It was established that furfurylideneacetophenone adds to the organomagnesium compound at the 1,4-position of the conjugated system with the formation of saturated ketones. Saturated ketones are also obtained from furfurylideneacetone, but in lower yields, due to the formation of a considerable amount of tar. In the experiments using methylmagnesium iodide in the synthesis the products obtained from furfurylideneacetone were exclusively tars [3].

The reaction of some organomagnesium compounds with the ethyl ester of β-(2-furyl)-acrylic acid proceeds in the direction of forming unsaturated tertiary alcohols [6-8]. Data on the direction of reaction when the ethyl ester of β-(2-furyl)-acrylic acid is reacted with methylaminemagnesium halides, and also when furfurylideneacetone is reacted with methylmagnesium bromide, are absent in the literature.

The large amount of literature material that exists on organomagnesium syntheses employing α,β-unsaturated ketones and the esters of α,β-unsaturated acids of the ethylene series indicates that these reactions can proceed in different directions, depending on the nature of the starting carbonyl and organomagnesium compounds, and also on the conditions under which the reactions are run [4-6,9]. When methylmagnesium halides are employed many investigators note the predominant formation of unsaturated tertiary alcohols and the products of their dehydration [6, 10-12].

Our first experiments on the synthesis of 1-(2-furyl)-3-methyl-1-buten-3-ol, the same as the analogous experiments of N. Maxim [3], showed but slight success. Vacuum-distillation of the crude glycerinlike tertiary alcohol resulted in dehydration of the latter and the considerable formation of tar. The portion that distilled (33-40%) was a mixture of 1-(2-furyl)-3-methyl-1-buten-3-ol, 1-(2-furyl)-3-methyl-1,3-butadiene and water. By means of later experiments it was established that to achieve successful synthesis of 1-(2-furyl)-3-

-methyl-1-buten-3-ol via the reaction of methyl-containing magnesium halides with the above-indicated carbonyl compounds it is necessary to run the reaction at temperatures of around 0°. The reaction product should be decomposed by slow pouring over crushed ice under thorough stirring, and the ether solution of the tertiary alcohol should be washed with sodium thiosulfate solution, after which the alcohol is stabilized with a small amount of hydroquinone. In the vacuum-distillation of 1-(2-furyl)-3-methyl-1-buten-3-ol the temperature of the distillation flask should not be permitted to exceed 150-160°, since at higher temperature, as a rule, the alcohol suffers dehydration, accompanied by the formation of tar.

Freshly distilled 1-(2-furyl)-3-methyl-1-buten-3-ol is a nearly colorless, pale-yellow glycerinlike liquid, readily soluble in acetone, ether and benzene, less soluble in ethanol and practically insoluble in water. When stored the alcohol turns yellow and gradually acquires a cherry-red color. The tertiary alcohol obtained in different experiments differs somewhat in its index of refraction values, which can be due to the presence of small amounts of 1-(2-furyl)-3-methyl-1,3-butadiene. Vacuum-distillation in the presence of an iodine crystal results in easy dehydration of the alcohol; the distillate is a mixture of 1-(2-furyl)-3-methyl-1,3-butadiene, water and the tertiary alcohol.

The 1-(2-furyl)-3-methyl-1,3-butadiene isolated from the mixture of dehydration products is a quite mobile, strongly light-refractory, pale-yellow liquid. It is readily soluble in acetone, ether and benzene, poorly soluble in ethanol and insoluble in water. It shows a high exaltation of the molecular refraction, which is characteristic for furan compounds that contain a conjugated system of double bonds in the α-position [8]. Similar to other unsaturated compounds of the furan series, the substance is an unstable compound and when stored it gradually acquires a yellow color and becomes less mobile. As a thin layer in the air it shows comparatively rapid transition into semitransparent films that are difficultly soluble in acetone. With maleic anhydride it gives an adduct, in which, based on the analysis data, 1 mole of 1-(2-furyl)-3-methyl-1,3-butadiene is combined with 1 mole of maleic anhydride.

EXPERIMENTAL

I. Preparation of 1-(2-furyl)-3-methyl-1-buten-3-ol.

1. From furfurylideneacetone and methylmagnesium iodide. To an ethereal solution of methylmagnesium iodide, prepared from 9.7 g (0.4 mole) magnesium and 57 g (0.4 mole) methyl iodide in 100 ml absolute ether 27.2 g (0.2 mole) furfurylideneacetone (b.p. 119-121° at 20 mm; m.p. 38.5-40.0°), dissolved in 100 ml absolute ether, was slowly added with vigorous mechanical stirring and cooling. Addition of the ethereal solution of furfurylideneacetone was carried out drop-wise at such a rate that the temperature of the reaction mixture did not exceed +5°. The reaction mixture was stirred for 30 minutes at room temperature and for 3 hours with heating on a water bath. The reaction product was cooled to 0° and gradually in small portions was poured into a wide-necked flask on cracked ice (300 g). This operation was carried out slowly with careful stirring. The basic magnesium salts were decomposed by addition of 25% previously neutralized (with ammonia) ammonium chloride solution. The ethereal solution of 1-(2-furyl)-3-methyl-1-buten-1-ol was separated from the aqueous layer; the latter was twice extracted with 50 and 30 ml of ether. The ethereal solution of alcohol and the ethereal extracts were combined and twice washed with a 5% solution of sodium thiosulfate, a 1% solution of sodium bicarbonate and with water and then dried with anhydrous sodium sulfate in presence of 0.1 g hydroquinone. After driving off the ether, the residue (28.5 g) was vacuum-distilled at 20 mm. The following fractions were collected: 1st to 115°, 3.78 g; 2nd 115-116°, 19.02 g and residue (resin) was 3.9 g. The 2nd fraction was 1-(2-furyl)-3-methyl-1-buten-3-ol:

n_D^{20} 1.5225, d_4^{20} 1.0267, MR_D 45.24; calc. 43.33. EM_D 1.91.

Found %: C 70.83; H 8.08. M 149.2. $C_9H_{12}O_2$. Calculated %: C 71.03; H 7.95. M 152.2.

The reaction with semicarbazide for the presence of possible admixture of 2-(2-furyl)-4-pentanone proved negative.

2. From furfurylideneacetone and methylmagnesium bromide. Taken for synthesis of 1-(2-furyl)-3-methyl-1-buten-3-ol: 9.7 g (0.4 mole) magnesium, excess of methyl bromide and 27.2 g (0.2 mole) furfurylideneacetone. The carrying out of the reaction, decomposition of the reaction product, isolation and purification of the alcohol were carried out under the same conditions as for the synthesis in which methyl iodide was used. Upon distillation of 24.6 g of unpurified alcohol at 15 mm, the following fractions were collected: 1st to 107°, 0.8 g; 2nd 107-109°, 19.03 g and residue, 2.9 g. The 2nd fraction had the following constants:

n_D^{20} 1.5255, d_4^{20} 1.0271, MR_D 45.36; calc. 43.33. EM_D 2.03.

Found %: C 70.84; H 8.20. M 150.8. $C_9H_{12}O_2$. Calculated %: C 71.03; H 7.95. M 152.2.

3. From ethyl ester of β-(2-furyl)-acrylic acid and methylmagnesium bromide. The ethyl ester of β-(2-furyl)-acrylic acid was prepared according to the prescription given in [7]. β-(2-furyl)-acrylic acid was synthesized from furfurol by the Perkin reaction. From 12.2 g (0.5 mole) magnesium in 125 ml absolute ether, an excess of methyl bromide and 33.2 g (0.2 mole) ethyl ester of β-(2-furyl)-acrylic acid, dissolved in 75 ml dry ether, was obtained (as described before) 23.3 g unpurified alcohol. Vacuum-distillation yielded 12.8 g of 1-(2-furyl)-3-methyl-1-buten-3-ol, which in constants and elementary composition proved analogous to the alcohol prepared from furfurylideneacetone.

II. Preparation of 1-(2-furyl)-3-methyl-1,3-butadiene.

Experiment 1. Vacuum-distillation (at 130-140° and 20-21 mm) in presence of an iodine crystal of 11.0 g 1-(2-furyl)-3-methyl-1-buten-3-ol with an admixture of 1-(2-furyl)-3-methyl-1,3-butadiene yielded 7.3 g (66.4%) of a mixture of dehydration products. 2.6 g (23.6%) of resin remained in the distilling flask. The mixture of dehydration products was washed twice with 5% sodium thiosulfate solution, then with water and dried with anhydrous $CaCl_2$. Distillation of 3.54 g of impure substance in vacuum over metallic sodium yielded 1-(2-furyl)-3-methyl-1,3-butadiene (2.9 g) with b.p. 82-83° at 20 mm; n_D^{20} 1.5775. A second distillation in vacuum over metallic sodium yielded 2.2 g of substance with b.p. 82-83° at 20 mm.

n_D^{20} 1.5781, d_4^{20} 0.9595, MR_D 46.35; calc. 41.39. EM_D 5.01.

Found %: C 80.22; H 7.65. M 131.0. $C_9H_{10}O$. Calculated %: C 80.56; H 7.51. M 134.2.

Experiment 2. In the synthesis of 1-(2-furyl)-3-methyl-1-buten-3-ol from the ethyl ester of β-(2-furyl)-acrylic acid and methylmagnesium iodide, vacuum-distillation of 28.0 g of impure alcohol yielded 10.23 g (33.5%) of a mixture of dehydration products. Treatment of the latter by the method described in Experiment 1 yielded 6.3 g of 1-(2-furyl)-3-methyl-1,3-butadiene with b.p. 82-83° at 20 mm, n_D^{20} 1.5781.

III. Reaction of 1-(2-furyl)-3-methyl-1,3-butadiene with maleic anhydride.

A yellow coloration was observed upon mixing 0.036 mole 1-(2-furyl)-3-methyl-1,3-butadiene with 0.036 mole maleic anhydride. After complete solution of maleic anhydride, the temperature of the reaction mixture rapidly rose to 170°. When the temperature fell to 40°, to the rather immobile reaction product was added an equivalent volume of dry benzene and for completion of reaction the solution was heated on a boiling water bath for 30 minutes. Petroleum ether (b.p. 85-87°) was added in small portions to the solution (cooled to room temperature) until turbidity. The crystals which came down were filtered off, washed 3 times with small portions of ethyl ether and dried in the air. Yield 6.06 g (71.7%) of light-yellow acicular adduct crystals with m.p. 71-74°. Half (3.0 g) of the substance was recrystallized by solution in ethyl ether with subsequent addition of petroleum ether. The subsequently separated portions (1.15 and 0.6 g) of adduct crystals had m.p. 73-75°.

Found %: C 67.07; H 5.29. M 230.9. $C_{13}H_{12}O_4$. Calculated %: C 67.23; H 5.21. M 232.2.

The second half (3.0 g) of unrecrystallized adduct was converted to the corresponding dibasic acid. A weighed portion of the anhydride was dissolved with mild heating in 10% caustic soda solution. When 20% sulfuric acid was added to the filtered solution, a voluminous precipitate came down, which was separated off, washed with water and dried in air. Yield 2.55 g (78.9%) of light-yellow crystals of dibasic acid. During the determination of the melting point of the substance, the color gradually changed from light-yellow to yellow-brown and then (at 163-167°) the substance melted with reddening of the fusion. The melting point was indefinite and markedly varied with the rate at which the temperature was raised in the apparatus. This phenomenon was evidently due to partial dehydration of the dibasic acid.

A portion (1.55 g) of the acid was extracted three times with 25-ml portions of ethyl ether. Petroleum ether was added in several portions to the ethereal extract until turbidity and formation of crystals. After cooling for an hour at 0°, the crystals were separated off, washed with ethyl ether and dried in the air. Isolated 0.50 g (32.3% of initial) purified dibasic acid, which had m.p. 165-167° (with decomposition). After evaporation of the ether at room temperature, from the mother liquor was isolated 0.32 g (20.6%) more of crystals with m.p. 165-167° (with decomposition).

Found %: C 62.48; H 5.69. Equiv. 119.7. $C_{13}H_{14}O_5$. Calculated %: C 62.39; H 5.64. Equiv. 125.1.

SUMMARY

1. The synthesis of 1-(2-furyl)-3-methyl-1-buten-3-ol from furfurylideneacetone was described, and also

from the ethyl ester of β-(2-furyl)-acrylic acid.

2. The dehydration of 1-(2-furyl)-3-methyl-1-buten-3-ol gave 1-(2-furyl)-3-methyl-1,3-butadiene.

3. The diene synthesis of 1-(2-furyl)-3-methyl-1,3-butadiene with maleic anhydride gave an adduct, and from the latter the corresponding dibasic acid was obtained.

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THE β-CHLOROETHYLAMIDE OF NICOTINIC ACID

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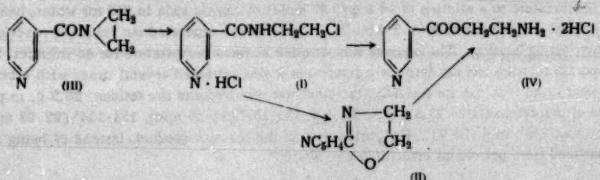
In searching for cancerolytic agents Drefahl and Konig recently synthesized the β-chloroethylamide of nicotinic acid (I), from which they later obtained 2-(3-pyridyl)-Δ^2-oxazoline (II) [1]. The appearance of this communication by the indicated authors aroused us to describe the experiments made in 1949 on the synthesis of the β-chloroethylamide of nicotinic acid by a different method. At the same time we are presenting the conditions used by us to convert this β-chloroethylamide into 2-(3-pyridyl)-Δ^2-oxazoline, giving better results than those used by Drefahl and Konig.

Basing ourselves on the statements made in the old study of Gabriel and Stelzner [2], in accord with which N-benzoylethyleneimine shows much easier opening of its three-membered ring under the influence of hydrogen halide acids than does ethyleneimine itself, we decided to synthesize various N-acyl derivatives of ethyleneimine and use them as alkylation agents in some of the cases of interest to us. Here it was revealed that among the other compounds obtained the N-nicotinoylethyleneimine (III) is unstable and, having been isolated from the reaction solution, shows comparatively rapid polymerization at room temperature. When an ether solution of the freshly prepared ethyleneimide of nicotinic acid is reacted with excess HCl solution in anhydrous alcohol the hydrochloride of the β-chloroethylamide of nicotinic acid is obtained in good yield, suffering easy



transformation into the dihydrochloride of the β-aminoethyl ester of nicotinic acid (IV) when its aqueous solution is boiled. Short heating of the hydrochloride of the β-chloroethylamide of nicotinic acid with the calculated amount of alkali in water solution yields 2-(3-pyridyl)-Δ^2-oxazoline, obtained in over 90% yield.

The pyridyloxazoline shows very slow change when heated with water and only after boiling for ~ 60 hours with a 12 to 15-fold amount of water does it show transformation into the β-hydroxyethylamide of nicotinic acid. In acid medium the oxazoline ring is easily opened even in the cold. Thus, the addition of the calculated amount of alcoholic HCl solution to an ether solution of the pyridyloxazoline yields, not the dihydrochloride of the pyridyloxazoline, as might be expected [3], but instead the dihydrochloride of the β-aminoethyl ester of nicotinic acid [4]; the water needed to realize this reaction is contained in sufficient amount in the solvents used.

EXPERIMENTAL

Ethyleneimide of nicotinic acid. The starting substance in the preparation of the ethyleneimide of nicotinic acid chloride was synthesized (Meyer and Graf [5]) by boiling nicotinic acid (45 g) with thionyl chloride (90 ml) for about 40 hours. The yield of acid chloride, separated by fractionation of the reaction solution was about 79%, b.p. 101-102° (21 mm), 122-123° (60-64 mm), m.p. 15-16°.

A solution (cooled to -12 to -15°) of 30.8 g (0.716 mole) of ethyleneimide in 150 ml of absolute ether was placed in a 3-necked flask (750 ml) fitted with mercury-sealed stirrer, thermometer and dropping funnel and to this was added drop-wise with stirring and ice-salt cooling 41 g (0.29 mole) of nicotinic acid chloride in 300 ml absolute ether at such a rate so that the temperature did not exceed -5 to -3°; the reaction mass was stirred at the same temperature for 3.5-4 hours more; the solution was decanted from the precipitate, not investigated further, which had separated out on the walls of the flask (probably ethyleneimine hydrochloride). This precipitate had to be immediately dissolved in water or else spontaneous polymerization soon set in with considerable evolution of heat, which was capable of breaking the flask. The ether was removed from the filtered solution in vacuum without access of atmospheric moisture at a temperature not exceeding 0°; the obtained white crystals of the ethyleneimide of nicotinic acid, due to its instability, was quickly used for the subsequent work. Yield of ethyleneimide 80-89%, on acid chloride.

The ethyleneimide of nicotinic acid was soluble in ether, benzene, alcohol and in water; at room temperature it turned into a transparent colorless liquid, which rapidly darkened and overnight was converted into a solid transparent substance, which was no longer soluble in ether.

β-Chloroethylamide of nicotinic acid. 35 g freshly-prepared crystalline ethyleneimide of nicotinic acid was dissolved in 200 ml absolute ether, filtered, if necessary, and gradually run into 350 ml 17.5% HCl solution in anhydrous alcohol with stirring at -5 to 0°. A white crystalline precipitate soon separated out. The next day the precipitate was separated off, washed with a small amount of anhydrous alcohol and absolute ether and dried in vacuum. Yield of β-chloroethylamide hydrochloride of nicotinic acid 44.6 g, m.p. 141-142°. After recrystallization from anhydrous alcohol (1:5), the melting point rose to 142-143°.

Found %: Cl (ion) 15.89; Cl (total) 31.77; N 12.74. $C_8H_9ON_2Cl \cdot HCl$. Calculated %: Cl (ion) 16.04; Cl (total) 32.07; N 12.67.

2 g of β-chloroethylamide hydrochloride of nicotinic acid was dissolved in 20 ml water and boiled for 1.5 hours. The solution was then steamed down in vacuum to dryness, the residue was dissolved with heating in 50 ml methyl alcohol and 100 ml hot ethyl acetate was added. Yield of β-aminoethyl ester dihydrochloride of nicotinic acid 1.3 g, m.p. 191-192°. After four precipitations from methyl alcohol with ethyl acetate, the melting point rose to 206-207° (decomp.).*

2-(Pyridyl-3)-Δ^2-oxazoline. 44.2 g (0.2 mole) of nicotinic acid β-chloroethylamide hydrochloride was added at room temperature to a solution of 16.8 g (0.42 mole) of caustic soda in 240 ml water, heated with shaking to 50° and held at this temperature for 3 minutes. The oil which separated out from the reaction mixture went into solution during heating. The mixture was set aside at room temperature for 45 minutes, 220 ml of ~ 50% caustic potash solution was run into the mixture and it was extracted several times with ether. The combined extracts were dried with calcined $MgSO_4$, the ether was removed, and the residue, 28.2 g, m.p. 67-69°, was distilled. Yield of pyridyloxazoline 27.3 g (92.2%), b.p. 135-137° (11-13 mm), 153-154° (22-23 mm), at atmospheric pressure about 260°, m.p. 70-71°. For purification of the reaction product, instead of being distilled, it may be recrystallized from petroleum ether with b.p. 80-100°.

Found %: C 65.19; H 5.77; N 18.94. $C_8H_8ON_2$. Calculated %: C 64.85; H 5.44; N 18.91.

Pyridyloxazoline was a colorless crystalline substance with a very faint odor, slightly like that of pyridine. It was readily soluble in water, alcohol, ether and benzene, sparingly soluble in the cold in petroleum ether. The aqueous solution gave a weakly alkaline reaction (on litmus).

To 0.5 g pyridyloxazoline in 30 ml water was added in the cold 225 ml of 1% aqueous solution of picric acid and the picrate, which separated out in the form of attached needles, was washed with water and dried in vacuum at room temperature and then with heating over P_2O_5 (100°, 3 hours), m.p. picrate 141-142°.

Found %: C 39.56; H 2.30; N 17.98, 18.40. $C_8H_8ON_2$. Calculated %: C 39.61; H 2.33; N 18.48.

To prepare the ethiodide, pyridyloxazoline was boiled with an excess of ethyl iodide and the crystalline precipitate which separated out was recrystallized from alcohol. M.p. 193-194° (upon lowering capillary into apparatus heated to 180°, rate of temperature rise 3° per minute). The ethiodide was readily soluble in water.

Found %: C 39.74; H 4.11; N 9.49; I 41.90. $C_{10}H_{13}ON_2I$. Calculated %: C 39.49; H 4.31; N 9.21; I 41.73.

A solution of 2 g pyridyloxazoline in 27.3 ml 1 N HCl was boiled under reflux for 1 hour and 45 minutes and steamed to dryness in vacuum. The obtained nicotinic acid β-aminoethyl ester dihydrochloride (2.3 g, m.p. 193-196° with decomposition) was purified by reprecipitation with absolute ether from anhydrous methanol;

*According to the data of Phillips and Baltzly, this compound has m.p. 213-214° [6].

m.p. 206.5-207° (decomp.). A mixed sample with the nicotinic acid β-aminoethyl ester dihydrochloride, prepared from nicotinic acid β-chloroethylamide gave no depression.

To a solution of 1 g pyridyloxazoline in 20 ml ether was added with stirring and cooling a mixture of 20 ml ether with 3.5 g 15.6% alcoholic solution of HCl and the precipitate of nicotinic acid β-aminoethyl ester dihydrochloride which separated out was purified by reprecipitation; yield 1 g, m.p. 206-207° (decomp.).

Found %: Cl 29.41. $C_9H_{13}O_2N_3 \cdot 2HCl$. Calculated %: Cl 29.67.

SUMMARY

A method was described for the preparation of the ethyleneimide, β-chloroethylamide and β-aminoethyl ester of nicotinic acid, and also for the preparation of 2-(3-pyridyl)-Δ^2-oxazoline.

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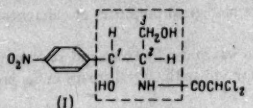
THE CHEMISTRY OF CHLOROMYCETIN (LEVOMYCETIN)

VIII. THE DEPENDENCE OF THE ANTIMICROBIAL ACTIVITY OF CHLOROMYCETIN ON ITS STRUCTURE AND THE MECHANISM OF CHLOROMYCETIN ACTION [1]

M.M. Shemyakin, M.N. Kolosov, M.M. Levitov, K.I. Germanova, M.G. Karapetyan, Yu.B. Shvetsov and E.M. Bamdas

The question of the dependence of the antimicrobial activity of D-threo-1-(p-nitrophenyl)-2-dichloroacetamido-1,3-propanediol (chloromycetin, chloramphenicol, levomycetin) on its structure and the closely associated question of the mechanism of the biological action of this compound are of considerable theoretical interest. The synthesis of several hundred analogs and derivatives of chloromycetin has been realized in recent years, in which connection many of the synthesized compounds have been subjected to biological testing, which permitted an elucidation of the different facets of the relationship between structure and the antimicrobial activity of chloromycetin to be approached. However, some of the conclusions made here proved to be based on faulty biological and stereochemical data (see [2], and also below), while many important facets of this relationship still remained completely without elucidation and in the very fore the basic question – what are the reasons and character of the influence shown by the individual groupings in the chloromycetin molecule on its activity.

The experimental data existing up to now have permitted making a sufficiently definite conclusion as to the degree and character of influence shown on the antimicrobial activity of chloromycetin only as regards the aminopropanediol portion of its molecule (I). Here attention was attracted to the fact that practically any structural or spatial changes of the aminopropanediol chain, changing either the nature or mutual distribution of the individual atoms and groupings in this portion of the molecule, lead to either complete or nearly complete loss of antimicrobial activity.*



(I)

*All three isomers of chloromycetin are practically inactive [3]. Substitution of alkyl groups for the hydrogen atoms at the O-, N- and C-atoms of the aliphatic chain [4-6], acylation of the hydroxyl groups [7], conversion of the primary alcohol group into either the carboxyl [8] or a carbalkoxyl group [6,9], etc., all lead to loss of in vitro activity. To be sure, in vivo the O-acyl derivatives of chloromycetin can show some activity in the presence of the corresponding esterases in the macroorganism; however, in this case the antimicrobial action is determined, not by the starting substance, but instead by the chloromycetin that is formed in its cleavage [10]. Recently [11] a slight antibacterial activity was shown for two of the chloromycetin analogs, containing at either C^1 or C^3 a chlorine atom in place of the hydroxyl group, which is probably due to the slight difference in the polarity and dimensions of the Cl atom and the OH group.

From this it was natural to arrive at the conclusion that the aminopropanediol chain of chloromycetin serves to bind it to specific proteins of enzymes, necessary for the normal metabolic activity of microorganisms. A group of English investigators [5] were the first to come to this conclusion in 1952; they believed that it was specifically as the result of this type of reaction between chloromycetin and the microbe cells that the normal exchange processes of the latter were disturbed. In the development of their hypothesis the indicated investigators also enunciated a number of further considerations relative to the reasons and character of this reaction, which, however, in our opinion, cannot be taken into consideration, since they were made on the basis of an incorrect space model for chloromycetin* and inaccurate results for a portion of the microbiological tests ([2] and below).

If we start with the correct space model for chloromycetin (Fig. 1) and at the same time take into consideration the fact that its molecule possesses a stable cis-conformation,** then a very peculiar characteristic of this compound becomes very strongly evident, namely, the exclusively close spatial proximity and at the same time the spatial availability of its acetamido and hydroxyl groups, which creates the possibility of their vigorous reaction with the peptide groups of protein molecules.*** As a result, the amide and the two hydroxyl groups in the aliphatic chain of chloromycetin specifically form that active center (dotted triangle in Fig. 1) which assures the addition of this molecule to the specific centers of certain bacterial enzymes, in that way excluding the latter from the normal exchange processes inherent to microbe cells.

What is the nature of the role played by the other two, no less important, portions of the chloromycetin molecule, namely the p-nitrophenyl radical and the N-dichloroacetyl residue, both of which are met very rarely in natural compounds? The question of the reason for the strong influence shown by these groupings on the antimicrobial activity of chloromycetin has hardly been discussed in the literature.**** It seemed most probable to us that the influence of both groupings should be associated with their characteristically strong polarizing action, and that it is specifically this property, together with the structural and spatial characteristics shown by the aminopropanediol portion of the molecule, that appears as one of the basic factors responsible for the high specificity shown by the biological action of chloromycetin.

To verify the validity of this postulation it was necessary to study the antimicrobial activity of two groups of chloromycetin analogs, differing from the former by the presence of substituents other than either the nitro group or the dichloroacetyl residue (compounds of Type II and III). Here it was very important to make sure that any of the mentioned changes in the chloromycetin molecule were not accompanied by any other changes in its structure; in particular, the spatial configuration should remain unchanged in all cases. In connection with this we developed in 1952-1953 two general methods for the synthesis of chloromycetin analogs of Type (II), possessing the same configuration as chloromycetin itself. With the aid of these methods we synthesized a number of analogs of this type [14-16], and then we studied the degree of their antimicrobial activity with respect to typical gram-positive and gram-negative bacteria. In most cases the synthesis of the various N-acyl analogs of chloromycetin of Type (III) failed to present any special difficulties (see EXPERIMENTAL), since based on

*By error the English investigators constructed a Stewart model, not of chloromycetin itself, but instead of its erythro isomer, and their evaluation of the biological properties of chloromycetin was based on the specific characteristics shown by this model.

**The cis-conformation of chloromycetin was shown by Fodor and coworkers [12].

***The specific arrangement of the acetamido and hydroxyl groups in the bromamphenicol crystal was first shown by Dunitz [13].

****The above-mentioned English investigators [5] only emphasized that the dichloroacetyl residue shows high specificity and cannot suffer any changes. As regards the less specific p-nitrophenyl radical, then due to the presence of a polar nitro group the latter should fulfill, in their opinion, the role of an "anchor", holding the chloromycetin molecule to the protein surface of the enzyme. Both of these statements are wrong. The first one contradicts the data on the considerable activity shown by certain analogs of chloromycetin when the N-acyl residue is changed ([2] and below). The second statement is not true for the reason that the antimicrobial activity of chloromycetin was found to depend, not on the local polarity of the nitro group, but instead on its polarizing action on the aliphatic chain of the molecule (see below).

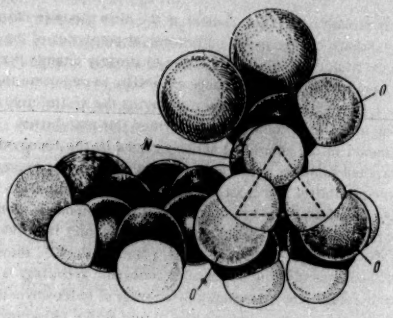
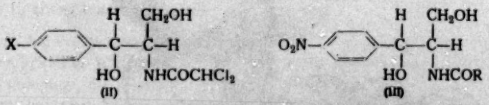


Fig. 1.

the methods [2] described in the literature the acylation of D-threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol is run under conditions that exclude the possibility of either inversion or racemization. The chloromycetin analogs that we obtained in this manner were also subjected to microbiological testing.



(II) (III)

The data given in the table on the degree of antimicrobial activity shown by the (II) type of chloromycetin analogs permit arriving at the conclusion that here the p-nitrophenyl radical shows great influence on the antimicrobial activity of the molecule, both in view of its electron nature and also due to the possible manifestation of its polarizing action. At the same time the geometric dimensions of this portion of the molecule, in contrast to the aminopropanediol grouping, fails to show decisive significance. Actually, it was revealed that the nitro group can be shifted along the system of conjugated multiple bonds without essential reduction in activity, while at the same time the absence of this conjugation leads to either slight or completely inactive analogs. Thus, for example, compounds of Type (II), with X equal to either p-$O_2NC_6H_4N$=N (No. 1) or p-$O_2NC_6H_4CH$=N (No. 2), show extremely high activity, while their close chloromycetin analogs, but devoid of the nitro group [II; X equal to either C_6H_5N=N (No. 3) or C_6H_5CH=N (No. 4)], and also (II) compounds with X = p-$O_2NC_6H_4CONH$ (No. 5), in which a continuous system of conjugated multiple bonds is absent between the nitro group and the aminopropanediol chain, are active only to slight degree. Also characteristic is the fact that the (II) compound with X = m-$O_2NC_6H_4N$=N (No. 6), appearing as the "meta-isomer" analog of chloromycetin [17], is comparable to the latter in the vigor of its antimicrobial action.

The above conclusion as to the character of the influence shown by the p-nitrophenyl residue on the antimicrobial activity of chloromycetin is further confirmed by the results obtained in the biological testing of a number of its other Type (II) analogs. Thus, it was found that these compounds most frequently show the greatest degree of loss in activity with lower electron-acceptor properties possessed by substituent X, found in the p-position of the benzene ring; and that in their influence on the antimicrobial activity these substituents can be arranged in the following order:*

$$NO_2 > CN > COOCH_3 > Cl > SO_2CH_3 > SO_2NH_2.$$

To be sure, a completely satisfactory parallelism is not observed here, since suppression of various microorganisms by antibacterial agents, showing at the same time both comparable and different properties, should proceed somewhat differently; for example, in the case of gram-negative bacteria the groupings CH_3S and CH_3O prove

*See the table for a comparison of the activity shown by chloromycetin and Compounds Nos. 7-11.

to be outside the presented series (see [18, 19] and Compound No. 12). Consequently, the presented series is to a certain degree conditional, although the general tendency noted here is undoubtedly valid.

Finally, it seemed extremely probable that replacement of the nitro group in chloromycetin by diverse ionogenic groupings would lead to a sharp change in the antimicrobial properties of the substance, due to the appearance of an ionic charge in the molecule. This charge should strongly change the capacity of the substance to be absorbed by proteins, and in this way also change its ability to penetrate through biological media and attach itself to specific bacterial enzymes. The results of studying the antimicrobial properties of the corresponding Type (II) analogs of chloromycetin completely confirmed this postulation. It was revealed that independent of the strength and character of the polarizing action exerted by the ionogenic groupings, their replacement of the nitro group always led to either nearly or completely inactive compounds. At the same time the elimination for the latter of the possibility to dissociate into ions was accompanied in most cases by the appearance of variable antimicrobial activity. For example, Type (II) compounds, containing X = COOH, SO_3H, SO_3H, AsO_3H_2, OH or NH_2 (Nos. 13-18), are either nearly or completely inactive, while the derivatives of these compounds, having X = $COOCH_3$, SO_2CH_3, SO_2NH_2, OCH_3 (Nos. 8, 10-12), show noticeable, and at times even considerable activity. Consequently, the entrance of ionogenic groupings is always accompanied by destruction of the specific antimicrobial properties shown by analogs of chloromycetin.* The appearance of this rule permits terminating the searches being made to find highly active chloromycetin analogs among compounds containing groupings of ionogenic character.

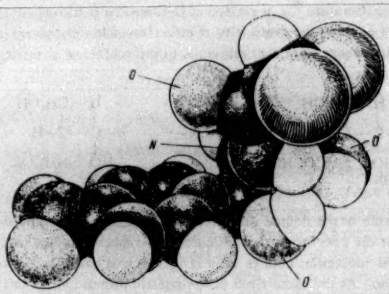


Fig. 2.

We will now pass to the question of the dependence shown by the antimicrobial activity of chloromycetin on the structure of its N-dichloroacetyl residue. This dependence bears a more complex character than for the case of the p-nitrophenyl radical, since, apparently, the acyl residue should not only manifest polarizing influence, but at the same time it should also satisfy certain definite geometric requirements. The need for the presence of substituents in the acyl residue, possessing a certain optimum polarity value, follows from the high activity shown by the Type (III) analogs of chloromycetin with R = either $CHBr_2$ or CH_2CN [20, 21], and by the sharply lower activity shown by the same type of analogs with R = either CCl_3 or CH_3 (see Compound No. 23, and also [21, 22]). At the same time the high activity shown by Compound (III) with R = $C_6H_4CHCl_2$-p is evidence that the dichloromethyl group, similar to the nitro group, can be shifted along the system of conjugated multiple bonds, and consequently not only the polarity, but also the polarizing influence exerted by the dichloromethyl group, is important for the molecule to manifest antimicrobial activity. A similar, although less clear picture is also observed when the three analogs of Type (III) with R = CCl_3, $CH{=}CHCCl_3$ or $CH_2CH_2CCl_3$ (Nos. 23-25) are compared: here Compound No. 24 shows only slightly lower activity than does Compound No. 23, whereas when compared with the last Compound No. 25 it already shows noticeably less activity. However, Compound

*The low activity shown by Type (II) compounds with X = $C_6H_5CH{=}N$ (No. 4), is probably due to the ionogenic characteristics of the substituents, since some activity shown by Type (II) analogs of chloromycetin with X equal either p-$HOC_6H_4N{=}N$ or m,p-$(O_2N)(HO)C_6H_3N{=}N$ (Nos. 21 and 22) is associated with the tendency shown by these compounds to exist in the quinoid form.

(III) with R = CH=CHCHCl$_2$ (No. 26) proved to be considerably less active than chloromycetin, although the removal of the dichloromethyl residue by one vinylene group should have failed to essentially change the electron character of the amide grouping.* Evidently, compliance with some sort of geometric requisites, essential on the basis that the N-acyl grouping is situated in direct proximity to the active center of the chloromycetin molecule, thus assuring its addition to bacterial enzymes, fails to be observed in this case. Apparently, the dichlorocrotonyl residue proved to be unsatisfactory as regards its geometric dimensions and shapes, either due to the fact that it functions as a screen for this active center, making its spatially inaccessible (see Fig. 2), or for the reason that it changes the conformation of the molecule, in this way depriving the aminopropanediol grouping of its inherent specificity as regards reaction with the peptide groups of protein molecules. From this it follows that the geometric character of the N-acyl residue is no less, and possibly even more essential than its polarizing influence.

As a result, the highly selective biological action shown by chloromycetin on microbe cells is simultaneously determined by three factors: 1) the strong polarizing action of the p-nitrophenyl radical, the geometrical dimensions of which fail to possess essential significance; 2) the strong polarizing action of the dichloroacetyl residue, which at the same time should also satisfy certain definite geometrical requirements; and 3) the strictly defined geometric dimensions and corresponding conformation of the aminopropanediol grouping. The polarizing action of the p-nitrophenyl radical, found at C^1 of the aliphatic chain, should be essentially reflected in the electron character of this carbon atom and its attached hydroxyl group, whereas the polarizing influence shown by the dichloroacetyl residue will first of all be sharply expressed relative to the electron character of the nitrogen atom, found at C^2 of the chain, in which connection considerable reduction in the electron density should exist in both cases. The coupling of these characteristics with a definite spatial proximity and availability shown by the acetamido and hydroxyl groups evidently determines the strong reactivity shown by these groups with specific peptide groupings of certain enzymes, necessary for the normal metabolic activities of microorganisms, which in the final end leads to disruption of the exchange processes for the latter.

To the extent that the necessary reduction of the electron density for the N- and O-atoms of the acetamido and hydroxyl groups can be achieved to varying degrees as the result of the polarizing influence exerted by various atoms and groupings, the relatively slight specificity shown by the p-nitrophenyl and dichloroacetyl radicals, which in some cases can be successfully replaced by other radicals with comparable polarizing action, becomes understandable. The reason is also clear why these radicals should not contain ionogenic groupings, since the transformation of a polar molecule into the ionic state (irrespective of whether it is positive or negative) sharply changes its ability to react with the protein constituents of enzymes, leading to nonspecific association with proteins due to electrostatic interaction of the ionic charges.

It is hoped that the theories developed here on the reasons, character and mechanism of disruption shown by chloromycetin on the normal metabolic exchange processes of microbe cells will facilitate further elucidation of this whole community of complex and multiphase phenomena.

EXPERIMENTAL

Preparation of D,L-threo-1-(p-nitrophenyl)-2-(γ,γ,γ-trichlorocrotonylamino)-1,3-propanediol (III, R = = CH = CHCCl$_3$). 6 g of D,L-threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol, 7.2 g methyl ester of γ,γ,γ-trichlorocrotonic acid [37] and 4 ml isoamyl alcohol were heated to 110° and after solution of the aminodiol precipitate, this temperature was held for 5 minutes more. The reaction mass was dissolved in ethyl acetate, washed with 0.1 N H_2SO_4 and with water. From the sulfuric acid solution was separated 1.5 g initial aminodiol with concentrated NH_3, and after treatment with charcoal and drying over Na_2SO_4, fractional precipitation with heptane yielded D,L-threo-1-(p-nitrophenyl)-2-(γ,γ,γ-trichlorocrotonylamino)-1,3-propanediol from ethyl acetate solution. Yield 17%; m.p. 165-166° (from dichloroethane).

Found %: C 40.65; H 3.43. $C_{13}H_{13}O_5N_2Cl_3$. Calculated %: C 40.67; H 3.39.

Preparation of D,L-threo-1-(p-nitrophenyl)-2-(γ,γ,γ-trichlorobutyrylamino)-1,3-propanediol (III, R = = $CH_2CH_2CCl_3$). To 6 g of D,L-threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol in 350 ml ether and 190 ml 0.5 N KOH was added with shaking in the course of 10 minutes a solution of 6.1 g γ,γ,γ-trichlorobutyryl chloride in 15 ml absolute ether (the acid chloride was prepared by heating γ,γ,γ-trichlorobutyric acid [38] with

*It should be mentioned that Compounds Nos. 27 and 28 show extremely similar activity, due to isomerization of the second compound into the first under the conditions employed in the microbiological testing, run at a solution pH above 7.

a 7-fold quantity of $SOCl_2$; yield 70%, b.p. 97° at 40 mm for 6 hours). The mixture was shaken for 30 minutes more, the ethereal solution was washed with 0.1 N H_2SO_4 and water, dried with Na_2SO_4 and concentrated. Yield of D,L-threo-1-(p-nitrophenyl)-2-(γ,γ,γ-trichlorobutyrylamino)-1,3-propanediol 87%; m.p. 116-117° (from dichloroethane).

Found %: C 40.58; H 3.94. $C_{13}H_{15}O_5N_2Cl_3$. Calculated %: C 40.46; H 3.89.

TABLE

Antibacterial Activity of Chloromycetin Analogs •

Expt. Nos.	Structure	Configuration	Activity relative to chloromycetin (in mole%) against				Literature	
			Staphylococcus aureus	*Bacterium coli*	*Bacillus subtilis*	*Vibrio fluorescens*	on the synthesis	on the biological testing
	Chloromycetin (I)	*D*	100	100	100	100		
	X in Formula II							
1	$-N=NC_6H_4NO_2$-p	*D*	105	< 45	105	20	[15]	
2	$-N=CHC_6H_4NO_2$-p	*D*	< 25	< 45	25	4	[15]	
3	$-N=NC_6H_5$	*D*	6	2	9	2.5	[16]	
4	$-N=CHC_6H_5$	*D*	< 0.5	1	4	1	[16]	
5	$-NHCOC_6H_4NO_2$-p	*D*	5	2	3	0.7	[16]	
6	$-N=NC_6H_4NO_2$-m	*D*	39	3.5	35	5	[16]	
7	$-CN$	*D*	25	95	10	10	[14, 15] [24—26]	[24, 25]
8	$-COOCH_3$	*D*	10	17	23	45	[16]	
9	$-Cl$	*D*	10	20	10	4	[14, 15, 17] [27—29]	[17, 27] [28]
10	$-SO_2CH_3$	*D*	11	9	4	20	[16, 18, 30]	[18]
11	$-SO_2NH_2$	*D*	11	2	2	18	[16]	
12	$-OCH_3$	*D*	5.5	45	4.5	10	[16, 19, 31] [32]	[19, 31]
13	$-COOH$	*D*	< 0.4	< 0.5	< 0.4	0.05	[14, 15]	
14	$-SO_3H$	*D*	< 0.2	< 0.2	< 0.1	< 0.1	[16]	
15	$-SO_3Na$	*D*	< 0.5	< 0.1	< 0.3	0.2	[16]	
16	$-AsO_3H_2$	*D*	< 0.2	0.1	< 0.1	0.1	[14, 15]	
17	$-OH$	*D*	< 0.4	1	0.7	0.4	[14, 15, 33]	
18	$-NH_2 \cdot HCl$	*D*	0.8	8	1	0.8	[14, 15, 34]	[35]
19	$-NHCOCH_3$	*D*	0.5	1	< 0.3	0.2	[16]	
20	$-NHCOC_6H_5$	*D*	2.5	1	10	2.5	[16]	
21	$-N=NC_6H_4OH$-p	*D*	6	1.5	9	5	[16]	
22	$-N=NC_6H_3(NO_2)(OH)$-m,p	*D*	5	< 2	14	7	[16]	
	R in Formula III							
23	$-CCl_3$	*D,L*	8.5	1.5	10	7	[20, 21, 36]	[20, 21]
24	$-CH=CHCCl_3$	*D,L*	5.5	< 3	4	3	••	
25	$-CH_2CH_2CCl_3$	*D,L*	4	< 0.8	2.5	1.1	••	
26	$-CH=CHCHCl_2$	*D*	8	1.5	5.5	4.5	••	
27	$-CH=CHCHCl_2$	*D,L*	4	< 2.5	2.5	2.5	••	
28	$-CH_2CH=CCl_2$	*D,L*	6	0.9	4	3.5	••	

•The antibacterial activity of the chloromycetin analogs was determined by the method of serial dilutions. The nutrient medium was beef-peptone broth with pH 7.2-7.4. The accuracy of the determinations was ±25%.

To 5 ml of the nutrient medium, seeded with 0.1 ml of a suspension of a 24-hour agar culture of the microorganism in physiological solution (the final concentration of the microbe cells in the seeded medium was 200,000 per ml), was added a water solution of the studied substance; if the latter showed low antimicrobial activity, then it was dissolved directly in the beef-peptone broth. Compounds Nos. 1-6, 14, 20 and 22-28 showed insufficient solubility in water; consequently, they were dissolved in alcohol, and the solution was diluted with either water or the broth to a 5% alcohol content. The control experiments with chloromycetin revealed that such an alcohol concentration fails to either influence the antibacterial activity value possessed by the substance or to inhibit the growth of the microbes.

••See the EXPERIMENTAL portion of this paper.

Preparation of D-,L- and D,L-threo-1-(p-nitrophenyl)-2-(γ,γ-dichlorocrotonylamino)-1,3-propanediol (III, R = CH = CHCHCl$_2$). To 9 g of D- or L-threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol in 550 ml ether and 275 ml 0.5 N KOH was added in the course of 20 minutes with shaking 7.4 g γ,γ-dichlorocrotonic acid chloride, dissolved in 20 ml absolute ether (the acid chloride was prepared by heating γ,γ-dichlorocrotonic acid* with a 5-fold quantity of $SOCl_2$; yield 85%, b.p. 79-81° at 15 mm, n_D^{20} 1.5155). Subsequent treatment of the reaction mass was carried out as in the preceding experiment. In absence of seeding, the substance crystallized only with great difficulty. Yield 70-75%.

D-threo-1-(p-nitrophenyl)-2-(γ,γ-dichlorocrotonylamino)-1,3-propanediol; m.p. 84-85° [from mixture of ethyl acetate and dichloroethane (1:5)], $[\alpha]_D^{20}$ -70.8° (c = 9.6 in acetone).

Found %: C 44.58; H 4.20. $C_{13}H_{14}O_5N_2Cl_2$. Calculated %: C 44.71; H 4.04.

L-threo-1-(p-nitrophenyl)-2-(γ,γ-dichlorocrotonylamino)-1,3-propanediol: m.p. 84-85°, $[\alpha]_D^{20}$ +67.6° (c = 10.0 in acetone). Found %: C 44.85; H 4.26.

D,L-threo-1-(p-nitrophenyl)-2-(γ,γ-dichlorocrotonylamino)-1,3-propanediol was prepared by mixing the D- and L-isomers and subsequent recrystallization from a mixture of ethyl acetate and dichloroethane (1:2). M.p. 144-145°. Found %: C 45.01; H 4.10.

Preparation and properties of D,L-threo-1-(p-nitrophenyl)-2-(γ,γ-dichlorovinyl acetamido)-1,3-propanediol (III; R = $CH_2CH = CCl_2$).

a) Preparation. To a solution of 6 g D,L-threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol in 300 ml anhydrous dioxane with stirring and at a temperature not exceeding 12-15° was added in the course of 30 minutes a solution of 2.45 g γ,γ-dichlorovinylacetyl chloride [39,40] in 25 ml dioxane. The mixture was stirred for 30 minutes more, filtered and concentrated in vacuum. The residue was dissolved in 50 ml ethyl acetate, washed with 0.1 N H_2SO_4 and 20% NaCl solution, dried with Na_2SO_4, the ethyl acetate was driven off in vacuum, the remaining oil was dissolved in 15 ml hot dichloroethane and seeded upon cooling with the crystals obtained by rubbing oil with dichloroethane and heptane on a watch glass. Yield of hydrate of D,L-threo-1-(p-nitrophenyl)-2-(γ,γ-dichlorovinylacetamido)-1,3-propanediol 88%, m.p. 72-73° (from 1:5 dichloroethane-ethyl acetate mixture). To remove the water of crystallization, the substance was dried at 100° and 1 mm to constant weight.

Found %: C 42.67; H 4.42; N 7.89; Cl 19.40; H_2O 5.03. $C_{13}H_{14}O_5N_2Cl_2 \cdot H_2O$. Calculated %: C 42.51; H 4.35; N 7.62; Cl 19.34; H_2O 4.90.

b) Isomerization. To a solution of 0.2 g D,L-threo-1-(p-nitrophenyl)-2-(γ,γ-dichlorovinylacetamido)-1,3-propanediol in 1 ml anhydrous dioxane was added 2 drops of dry triethylamine; the mixture was set aside for 45 hours and evaporated down in vacuum. Yield of D,L-threo-1-(p-nitrophenyl)-2-(γ,γ-dichlorocrotonylamino)-1,3-propanediol 90%, m.p. 144-145° (from mixture of ethyl acetate and dichloroethane).

c) Hydrolysis. 1.5 g of D,L-threo-1-(p-nitrophenyl)-2-(γ,γ-dichlorovinylacetylamino)-1,3-propanediol and 15 ml 20% HCl were boiled for 2 hours, cooled, 10 ml water was added and this was followed by chloroform extraction. After evaporation of the extract, 0.58 g of γ,γ-dichlorovinylacetic acid was obtained; yield 87%; m.p. 42-43° (from hexane). From hydrochloric acid solution concentrated NH_3 separated out 0.83 g D,L-threo-1-(p-nitrophenyl)-2-amino-1,3-propanediol. Yield 91%, m.p. 142-144° (from water).

SUMMARY

A number of N-acyl analogs of chloromycetin were synthesized, which together with the earlier obtained p-substituted D-threo-1-phenyl-2-dichloroacetamido-1,3-propanediols were subjected to microbiological testing against gram-positive and gram-negative organisms. On the basis of the obtained data we discussed the relationship between the structure and the antimicrobial activity of chloromycetin, the reasons and character of influence shown by the individual groupings of the chloromycetin molecule on this activity, and also the mechanism of the first stages for the reaction of chloromycetin with bacterial enzymes.

*Two γ,γ-dichlorocrotonic acids were previously described in the literature: with m.p. 42-43° [40] and with m.p. 100-101° [41]. Recently A.N. Nesmeyanov et al. [39] showed that only the second of these compounds is γ,γ-dichlorocrotonic acid, since the first is an isomer of γ,γ-dichlorovinylacetic acid. We discovered that the γ,γ-dichlorobutyric acid described in literature with m.p. 103-104° [42] is in reality γ,γ-dichlorocrotonic acid (the latter and its amide were identified by mixed melting points with the corresponding substances, prepared by the method of A.N. Nesmeyanov et al. [39]).

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THE SYNTHESIS OF DIHEXYLFLUORESCEIN

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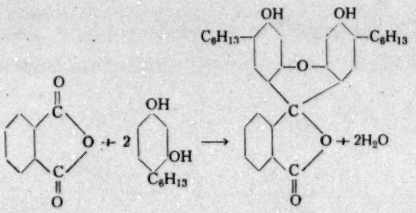
Hexylresorcinol (4-n-hexyl-1,3-dihydroxybenzene) finds extensive use in medicine, and especially in veterinary practice, as one of the more active anthelmintic preparations. Phenols show the ability to condense with phthalic anhydride, forming phthaleins, which, like their simplest member, phenolphthalein, also prove effective in both human and animal organisms.

It seemed of interest to us to obtain from hexylresorcinol and phthalic anhydride a similar condensation product in the hopes that being simultaneously a derivative of hexylresorcinol and phenolphthalein, it might show higher pharmacological activity than the latter.

To obtain phthaleins the phenols are heated with phthalic anhydride at 120° in the presence of water-removing agents, for example anhydrous zinc chloride or concentrated sulfuric acid. Some phenols, in particular resorcinol and its substituted derivatives, condense with phthalic anhydride under direct heating with the latter at 200° in the absence of water-removing agents.

For our experiments we started with hexylresorcinol of pharmacopoeia grade, being a rose-colored solid with m.p. 67°. Prior to condensation it was recrystallized from benzene. The phthalic anhydride used by us was of the highest purity with m.p. 132°, for which reason it was not purified further.

Stoichiometric proportions of hexylresorcinol and phthalic anhydride were heated at 200°. We failed to observe the formation of a condensation product even after heating the mixture for several hours. Gases with a disagreeable odor were evolved, and the phthalic anhydride sublimed. The residue was a hard carbonaceous mass, insoluble in the usual solvents. In our opinion, although the dihexylfluorescein can be formed under the given conditions in accord with the reaction:



still it suffers decomposition at 200°.

Gas evolution was not observed when 0.3 g of phthalic anhydride and 0.8 g of hexylresorcinol was heated in the presence of anhydrous zinc chloride at 110-120°. On cooling a dark brown mass was obtained, which dissolved in alkali with a bright orange, nearly red color and with an intensely green fluorescence. Acidification of the alkaline solution gives the substance as a precipitate which can be isolated. This substance is insoluble in water, and is slightly soluble in alcohol and benzene; it dissolves in concentrated formic acid and in ether. Reddish-brown crystals with m.p. 105° are obtained after recrystallization from ether. Yield 0.73 g (73%).

Heating of hexylresorcinol with phthalic anhydride at 110-120° in the presence of concentrated sulfuric acid yields the same product, but its yield is raised to 98%.

Found %: C 76.55, 76.59; H 7.34, 7.39. $C_{32}H_{36}O_5$. Calculated %: C 76.77; H 7.25.

SUMMARY

1. The condensation of hexylresorcinol with phthalic anhydride at 110-120° in the presence of either anhydrous zinc chloride or concentrated sulfuric acid gave the previously unknown dihexylfluorescein.

2. In contrast to other resorcinol derivatives, hexylresorcinol fails to give the phthalein when heated with phthalic anhydride at 200° in the absence of water-removing agents.

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PREPARATION OF 10-VINYLACRIDONE

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10-Alkylacridones are substitution products of the hydrogen found on the nitrogen atom in acridones. The best known of the 10-alkylacridones are the 10-methylacridones. The first member of this series was first obtained by Decker [1] in 1892 from acridine. This synthesis was repeated in 1899 [2], and in 1914 it was improved considerably [3]. Further improvement of the Decker method permitted achieving a good quantitative yield [4]. Some of the derivatives of the 10-alkylacridones, possessing valuable pharmaceutical properties, aroused great interest and were subsequently studied by a number of authors [5]. The 10-ethylacridones have also been described, but they have been studied to a considerably lesser degree [6].

We prepared 10-vinylacridone, a compound not described in the literature. Syntheses in this direction make it possible to obtain a number of previously unknown compounds.

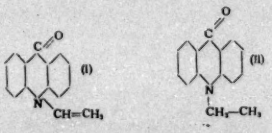
EXPERIMENTAL

Preparation of 10-vinylacridone (I). 11 g acridone (prepared by Graebe's method [7]) dissolved in 250 ml n-butyl alcohol or in 150 ml dioxane, was vinylated in a 1 liter rotating autoclave by the method of A.E. Favorsky and M.F. Shostakovsky [8] at 180° and 13 atm. initial pressure. 0.5 g powdered caustic potash was added to the reaction mixture as the catalyst. Vinylation was complete after 4-5 hours. When n-butyl alcohol was used as solvent, it was vinylated together with acridone and gave an almost theoretical yield of vinyl ether. Due to its sparing solubility in ethers, 10-vinylacridone was removed from the autoclave in a quite pure state. In its crude state it was in the form of light-yellow silky crystals with m.p. 180°. After recrystallization from benzene or alcohol, the pure 10-vinylacridone had m.p. 181.5°. Yield of product 10.2 g (92%).

Found %: N 6.37. $C_{15}H_{11}ON$. Calculated %: N 6.34.

10-Vinylacridone was a base, very readily soluble in alcohol, benzene, dioxane and in other organic solvents; difficultly soluble in ether. Its alcoholic solutions were light-yellow with a weak violet fluorescence.

For verification of structure of 10-vinylacridone, 10-ethylacridone (II) was prepared.



2 g of 10-vinylacridone, dissolved in 100 ml dioxane, was hydrogenated in the presence of 0.1 g skeletal nickel. Hydrogenation was carried out with shaking and at room temperature until addition of the calculated amount of hydrogen. The reaction was complete after 4-5 hours. After separation of the catalyst from the reaction mixture, 10-ethylacridone crystallized out from the filtrate upon addition of water. The obtained 10-ethylacridone was in the form of light-yellow prismatic crystals with m.p. 159° [6]. After multiple recrystallizations from alcohol, its melting point remained unchanged. A mixed sample gave no depression. Yield of product 1.9 g (94%).

Found %: N 6.34. $C_{15}H_{13}ON$. Calculated %: N 6.28.

10-Ethylacridone was a base, readily soluble in alcohol, dioxane, benzene and in other organic solvents. Its solutions were light yellow with a strong blue-violet fluorescence.

SUMMARY

A method was developed for the preparation of 10-vinylacridone; the yield of product was close to the theoretical. It was established that 10-vinylacridone can be easily and completely reduced to 10-ethylacridone.

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STRUCTURE AND CHEMICAL TRANSFORMATIONS OF ALKALI ORGANIC COMPOUNDS OF ANILS

II. THE TRANSFORMATIONS OF DISODIUM AND DILITHIUM COMPOUNDS OF BENZOPHENONE-PHENYLIMIDE UNDER THE INFLUENCE OF ALKYL HALIDES [1]

B.M. Mikhailov and K.N. Kurdyumova

According to Schlenk and Bergmann [2], the reaction of methyl iodide with disodium benzophenonephenylimide results in cleavage of the metal atoms and the starting anil is regenerated. Our study revealed that the reaction between disodium benzophenonephenylimide (I) and methyl iodide proceeds by a different path. It leads to the formation of a mixture of substances, testifying to the extremely peculiar and complex nature of the reaction course. The reaction products were shown to contain phenylbenzhydrylamine, formed in 25% yield when the metal atoms are replaced by hydrogen, and proving to be the only substance present in which the anil skeleton is retained. The remaining reaction products arise as the result of a parallel process, accompanied by rupture of the molecule at the carbon-nitrogen bond and leading in the finally to the formation of aniline (in 48% yield), 1,1-diphenylethylene (18%) and 2,2,3,3-tetraphenylbutane. In addition, gaseous substances are obtained in the reaction process, consisting mostly of methane and ethylene. An essential characteristic of the reaction is the consumption of methyl iodide, consisting, as opposed to the expected amount of two molecules, of about one molecule per molecule of alkali organic compound; and also the fact that only roughly half of the metal is converted to the halide, while the remaining portion of the metal, after the reaction mass is decomposed with water, appears as sodium hydroxide.

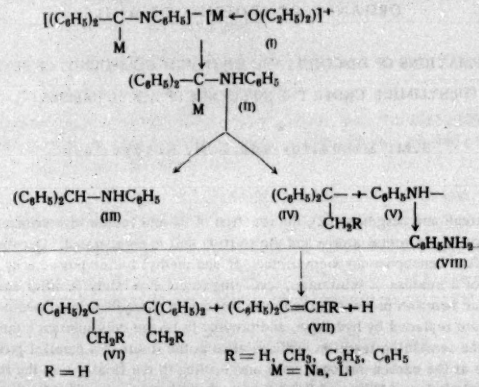
To study the influence of the nature of the alkali metal and of the halide in the methyl halide on the reaction course, appearing, for example, with much vigor in the anthracene series of dimetallic derivatives [3], we studied the reaction of the disodium compound of benzophenonephenylimide with methyl chloride, and of the dilithium compound with methyl chloride and methyl iodide. Here it was revealed that the nature of the metal and of the halide fail to exert too sharp an influence, being mainly manifested in the yields of phenylbenzhydrylamine and in the formation of considerably smaller amounts of gaseous hydrocarbons (Table 1).

The influence exerted by the nature of the radical in the halide compound on the course of the investigated process was studied in the reactions in which ethyl iodide, n-propyl iodide and benzyl chloride were used. It was revealed that the basic characteristics prevailing for the transformations of dimetallic derivatives of the benzophenone anil are fully retained when the higher halide derivatives are used. Specifically, in these cases also phenylbenzhydrylamine and aniline are obtained, while instead of 1,1-diphenylethylene the corresponding 1,1--diphenylpropylene (from C_3H_5I), 1,1-diphenylbutylene (from n-C_3H_7I) or 1,1,2-triphenylethylene (from benzyl chloride) is formed (Table 1). In contrast to the reaction with the methyl halide, in the experiments with the higher alkyl and aralkyl halides we failed to observe the formation of dimeric hydrocarbons, similar to 2,2,3,3--tetraphenylbutane.

It should be mentioned that reduction of alkali-metal organic compounds had been observed by us earlier in the reaction between the alkali organic derivatives of 9,10-dihydroanthracene and alkyl halides, and that this reaction is also accompanied by gas formation [3-4].

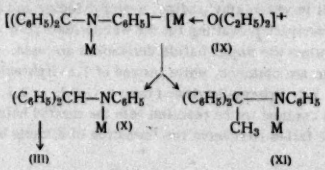
Our experimental data permit assuming the following scheme for the transformations shown by disodium benzophenonephenylimide under the influence of alkyl and aralkyl halides. At the base of this scheme lies the principle of consecutive entrance of the metal atoms into reaction and it is assumed, in accord with the well-known fact, that the ionized metal atoms show a greater reactivity than do the covalently bound atoms, and con-

sequently they are the first to enter into reaction. The dimetallic complex of benzophenonephenylimide, to which Structure (I) is assigned [1], is reduced in the first reaction stage; the ionized, more reactive metal atom being replaced here by hydrogen to form the monometallic Compound (II). The latter then suffers a double type of transformation. It is partly reduced further to the phenylbenzhydrylamine (III), while part of it exchanges the second metal atom for the alkyl group and simultaneously decomposes into Radicals (IV) and (V). Depending on its structure, the hydrocarbon Radical (IV) either completely loses its hydrogen and is transformed into the ethylene hydrocarbon (VII) or, in addition, suffers dimerization into the saturated hydrocarbon (VI) (2,2,3,3-tetraphenylbutane is obtained with CH_3X). Radical (V) is transformed into aniline (VIII).



To the extent that the structure of dimetallic compounds of anils can be depicted in the form of (IX), where the metal atom in the anion is covalently bound with the nitrogen atom, and not with the carbon, it is evident that an alternate scheme for the transformations of dimetallic compounds of anils is possible. With this alternate scheme the reaction of methyl iodide with (IX) yields the phenylbenzhydrylamine (III) by the path of consecutive hydrogenolysis of both metal atoms via the stage of forming the intermediate monometallic Compound (X). The other substances, 1,1-diphenylethylene, 2,2,3,3-tetraphenylbutane and aniline, can be obtained by the hydrogenolysis and simultaneous cleavage at the C–N bond of lithium 1,1-diphenylethylphenylamide (XI), showing parallel origin from (IX) by replacement of its ionized metal atom by the alkyl radical.

A choice between the two indicated methods can be made by studying the transformations of the monometallic Compound (XI) under the influence of an alkyl halide. For this purpose we obtained, with the aid of phenyllithium, Compound (XI) from 1,1-diphenylethylphenylamine and investigated its behavior toward methyl iodide. It was revealed that lithium 1,1-diphenylethylphenylamide (XI) under the influence of methyl iodide



suffers partial reduction to 1,1-diphenylethylphenylamine (III) (in 28% yield), while part of it exchanges its metal for the methyl group and at the same time suffers decomposition at the carbon-nitrogen bond, to yield as a result 1,1-diphenylethylene (54%), 2,2,3,3-tetraphenylbutane and methylaniline (50%):

(XI) $\xrightarrow{CH_3I}$ $(C_6H_5)_2C{=}CH_2 + C_6H_5NHCH_3 + (C_6H_5)_2C(H_3C)-C(C_6H_5)_2(CH_3)$.

The formation of methylaniline (and not aniline) from lithium 1,1-diphenylethylphenylamide (XI) serves as evidence that compound (XI) fails to figure as an intermediate product in the transformations shown by the dimetallic compounds of benzophenonephenylimide.

Consequently, Structure (IX) is excluded for the dimetallic compounds of anils. This demonstrates the validity of the structural formula (I) proposed for them and of the mechanism ensuing from this formula for the transformations occurring under the influence of alkyl halides.

EXPERIMENTAL

All operations with organometallic compounds were carried out in a nitrogen atmosphere.

To prepare the organometallic compounds, a mixture of benzophenone anil (20 g, 0.077 mole), metal (0.18 mole sodium or 0.25 mole lithium) and 200 ml ether was placed in a bottle with beads and shaken for 60-70 hours. On completion of shaking, the bottle was connected to a T-piece, through one end of which by means of a dropping funnel was added an ethereal solution of the halogen compound; the other end was connected to a gasometer. In the experiments with methyl chloride the first arm of the T-piece was also fitted with a tube, reaching almost to the bottom of the bottle, through which passed the stream of alkyl halide. When the reaction was complete, the reaction mass was filtered through a strainer from the excess of metal, washed with water, the ethereal solution was dried, the ether was driven off and the residue was treated as described below. The quantity of metal in the form of hydroxide and halide was determined in the aqueous solution by titration. The gaseous products were analyzed in an Orsat apparatus.

Reaction of methyl iodide with disodium benzophenonephenylimide. To a suspension of the organometallic compound was slowly added an ethereal solution of methyl iodide (11.4 g) and heat evolved, gaseous products were liberated and the reaction mass changed from dark-red to brown. The oily residue (20 g) obtained from the ethereal solution was treated with 100 ml 20% hydrochloric acid at the boil under reflux for 30 minutes. The reaction mass was then extracted with benzene, the insoluble phenylbenzhydrylamine hydrochloride was filtered off and the benzene solution, containing hydrocarbons, was separated from the hydrochloric acid solution.

Phenylbenzhydrylamine. The water-insoluble hydrochloride of the secondary amine was washed on a filter with benzene and water and dried. 6.4 g of salt formed with m.p. 188-190°. From methanol the salt crystallized in the form of colorless fine crystals with m.p. 189-190°. Yield 25%. The amine, separated from the salt, was distilled and crystallized from petroleum ether. B.p. 180-182° (2 mm), m.p. 56-57°.

Found %: C 88.03; H 6.77. $C_{19}H_{17}N$. Calculated %: C 87.98; H 6.61.

The substance gave no melting point depression in mixture with known phenylbenzhydrylamine (m.p. 57°), prepared by hydrolysis of disodiumbenzophenonephenylimide [5].

Aniline. The hydrochloric acid solution, obtained by treatment of the reaction products with hydrochloric acid, was alkalized, the oil was extracted with benzene and distilled. Yield 3.5 g (48.2%) aniline, b.p. 54-55° (2 mm), d_4^{20} 1.021, n_D^{20} 1.5847.

Found %: C 77.35; H 7.98; N 15.33. C_6H_7N. Calculated %: C 77.39; H 7.58; N 15.03.

The amine hydrochloride gave no depression with aniline hydrochloride.

1,1-Diphenylethylene. The solvent was driven off from the benzene extract, obtained after treatment of the reaction products with hydrochloric acid, and the residue was fractionated. Yield 2.6 g (18.6%) of 1,1-diphenylethylene; b.p. 102-105° (2 mm), d_4^{20} 1.0249, n_D^{20} 1.6084.

Found %: C 93.28; H 6.85. $C_{14}H_{12}$. Calculated %: C 93.29; H 6.71.

Oxidation of the hydrocarbon with sodium bichromate yielded benzophenone. Bromination of the hydrocarbon yielded 1,1-diphenyl-2-bromoethylene with m.p. 40-41° (a mixed sample with known 1,1-diphenyl-2-bromoethylene [6] gave no melting point depression).

2,2,3,3-Tetraphenylbutane. The residue from the distillation of 1,1-diphenylethylene (2.5 g) was chromatographed on aluminum oxide. Benzene and petroleum ether served as solvents. Yield 0.9 g crystalline substance, which after crystallization from alcohol had m.p. 126-127°. According to literature data, 2,2,3,3-tetraphenylbutane has m.p. 127° [7]. Yield of hydrocarbon 8%.

Found %: C 93.05; H 6.74. $C_{28}H_{26}$. Calculated %: C 93.18; H 6.82.

670 ml gaseous substances, consisting of 32% methane, 62.5% ethylene, 2.5% ethane and 2.5% acetylene, were obtained in the experiment.

The experimental results on the reaction of alkyl halides with dimetallic compounds of benzophenone anil are given in the table.

1,1-Diphenylethylphenylamine. To phenyllithium, prepared from 2.8 g lithium, 31.4 g bromobenzene and 100 ml ether, was added 16.3 g acetophenone anil, diluted with 20 ml ether. After boiling for 6 hours, the reaction mixtnre was treated with water, the solvent was driven off from the ethereal layer and the residue was vacuum-distilled. Yield 12.5 g (55%) of 1,1-diphenylethylphenylamine with b.p. 195-197° (4 mm) in the form of viscous yellow oil, which crystallized upon standing (m.p. 50-53°).

Found %: C 87.60; H 7.17. $C_{20}H_{19}N$. Calculated %: C 87.87; H 7.0.

TABLE

Starting substances		Yield (in %)				Yield of gas (in ml)
Dimetallic compound	RX	Phenylbenzhydrylamine	aniline	$(C_6H_5)_2C=CHR$	2,2,3,3-tetraphenylbutane	
Disodiumbenzophenone-phenylimide	CH_3Cl	32.6	50.0	20.0*	6.1	194
Dilithiumbenzophenone-phenylimide	CH_3Cl	37.5	52.6	26.4*	8.0	31
Ditto	CH_3I	18.4	50.9	28.0*	9.1	124
"	C_2H_5I	22.8	50.9	45.3**	–	36
Disodiumbenzophenone-phenylimide	C_2H_5I	32.2	50.9	32.0**	–	91
Ditto	$n\text{-}C_3H_7I$	35.3	54.1	35.3***	–	
Dilithiumbenzophenone-phenylimide	$C_6H_5-CH_2Cl$	15.2	59.6	55.7****	–	

*1,1-Diphenylethylene.

**1,1-Diphenylpropylene; m.p. 51-52° (literature data [8] give m.p. 52°). Found %: C 93.08; H 7.00. $C_{15}H_{14}$. Calculated %: C 92.74; H 7.26.

***1,1-Diphenyl-1-butene, b.p. 120-123° (2 mm), d_4^{18} 1.031, n_D^{18} 1.160. Found %: C 91.79; H 7.72. $C_{16}H_{16}$. Calculated %: C 92.25; H 7.75.

****1,1,2-Triphenylethylene, m.p. 71-72° (literature data [9] give m.p. 72-73°). Found %: C 93.59; H 6.55. $C_{20}H_{16}$. Calculated %: C 93.71; H 6.29.

The amine hydrochloride, crystallized from a chloroform-ether mixture, had m.p. 190-191° with decomposition.

Found %: N 4.53. $C_{20}H_{20}NCl$. Calculated %: N 4.51.

Reaction of methyl iodide with lithium 1,1-diphenylethylphenylamide. To the phenyllithium prepared from 9.4 g (0.06 mole) bromobenzene, 0.9 g lithium and 50 ml ether, was added with cooling an ethereal solution of 10 g (0.036 mole) 1,1-diphenylethylphenylamine. The reaction went with evolution of heat, the reaction mass colored dark-red.

To the obtained lithium compound of 1,1-diphenylethylphenylamine was added with ice-water cooling an ethereal solution of methyl iodide (5.2 g). The brown reaction mass was set aside for 2 hours and then treated

with water. Separation of the reaction products was carried out by the method used in the experiments with the dimetallic derivatives. Yield: 1) 3.1 g (28%) of 1,1-diphenylethylphenylamine hydrochloride, m.p. 190-191° (with decomposition); 2) 3.5 g (54.4%) of 1,1-diphenylethylene, b.p. 125-127° (1 mm).

Found %: C 92.92; H 6.74. $C_{14}H_{12}$. Calculated %: C 93.29; H 6.71.

3) 0.15 g (1.1%) 2,2,3,3-tetraphenylbutane (m.p. 126-128°); 4) 2.5 g (49.8%) methylaniline hydrochloride (m.p. 118-119°). Picrate, m.p. 142-143° (according to literature data m.p. 144.5°).

Found %: N 16.87. $C_{13}H_{12}O_7N_4$. Calculated %: N 16.65.

SUMMARY

1. Dimetallic compounds of benzophenonephenylimide suffer a series of consecutive and parallel transformations under the influence of either alkyl or aralkyl halides. The first stage of reaction consists in replacement of the ionized metal atom by hydrogen with the formation of a monometallic compound. The latter is then partially converted into phenylbenzhydrylamine, and partially exchanges its metal atom for the hydrocarbon radical, at the same time decomposing at the carbon-nitrogen bond with the formation of 1,1-diphenylethylene hydrocarbons, aniline and (when a methyl halide is used) 2,2,3,3-tetraphenylbutane.

2. Lithium 1,1-diphenylethylphenylamide under the influence of methyl iodide is partly reduced to 1,1-diphenylethylphenylamine, and partly replaces the metal by the methyl group with simultaneous decomposition at the carbon-nitrogen bond, in which connection methylaniline, 1,1-diphenylethylene and 2,2,3,3-tetraphenylbutane are formed.

The transformations shown by lithium 1,1-diphenylethylphenylamide serve as proof for the structure proposed for the dimetallic compounds of benzophenonephenylimide and for the mechanism of their transformations under the influence of alkyl halides.

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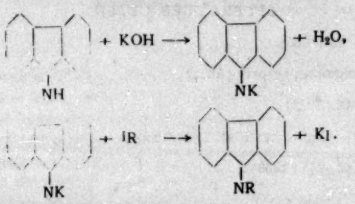
THE SYNTHESIS OF N-CARBAZOLEPROPENE OXIDE

F.M. Ezrielev and N.A. Larin

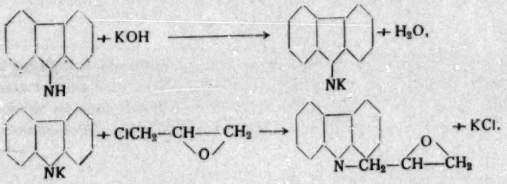
The N-alkylcarbazoles (N-methyl- and N-ethylcarbazoles) were first obtained by Graebe in 1880 [1]. At the present time a large number of quite different N-carbazole derivatives are known [2,3]. A German patent [4] was published in 1915, where, in searching for new dyes and pharmaceuticals, a product is described, obtained by reacting carbazole with epichlorohydrin at 250-260°. Nothing is given in the patent on the structure and characteristic constants of the product. The substance obtained in this patent is a dark oil, readily soluble in benzene and several other solvents. It is not disclosed whether the oxide ring of the epichlorohydrin remained untouched in the reaction or whether the process took place with its opening.

Our object in the present work was to obtain N-carbazolepropene oxide, i.e., a compound in which the oxide ring of epichlorohydrin is retained during reaction. To synthesize N-carbazolepropene oxide we essentially used the method of Levy [3], used by him to synthesize alkylcarbazoles, i.e., we reacted the proper alkyl iodide with potassium carbazole, previously obtained by the fusion of carbazole with potassium hydroxide:



However, our first attempt to obtain N-carbazolepropene oxide in this manner proved unsuccessful. The reaction is exothermic, for which reason complete tarring of the product occurred. Subsequently we reduced the concentration of the reacting components: the synthesis was run in a neutral solvent (either ether or benzene). Here the reaction proceeded smoothly, and only slight self-heating up to 30-35° was observed.

The synthesis of N-carbazolepropene oxide proceeded in two stages:



*R is alkyl, aryl, acetyl, etc. The alkyl bromides and chlorides can be used instead of the alkyl iodides.

EXPERIMENTAL

Synthesis of potassium carbazole. In an iron crucible (40 ml) was placed a mixture of 16.7 g (0.1 mole) carbazole and 5.6 g caustic potash. The crucible was heated to 220-250° and the cover was loosely closed; some of the carbazole sublimed. A brown fusion formed, which while still hot was poured out of the crucible; after hardening, this fusion was rubbed to a fine yellow powder which was kept in a hermetically sealed flask in a dry and dark place.

Condensation of potassium carbazole with epichlorohydrin. In a 0.25 liter flask was placed a solution of 30 ml epichlorohydrin in 100 ml dry benzene. To this was added 16-17 g dry potassium carbazole in fine portions. This operation was continued for 40-45 minutes; the flask was often shaken during this and from time to time placed in cold water to avoid excessive heating. The reaction mixture was then set aside for 15-20 hours and then 30-50 ml more of dry benzene was added. The precipitate of potassium chloride which formed upon standing was sucked off on a Buechner funnel and the yellow filtrate was washed with water and dried over $CaCl_2$. The benzene filtrate was then evaporated down in a porcelain cup on a sand bath and after removal of benzene and unreacted epichlorohydrin in this manner, the residue was subjected to 3-fold recrystallization from boiling alcohol. The product with m.p. 108-109° was collected. Yield of product was 24%, on initial carbazole.

The content of epoxyl group in the obtained product was determined by Schrade's method [5], which is based on the fact that the action of hydrochloric acid causes the 3-membered oxide ring to open:

$$HCl + RCH_2CH\!-\!CH_2 \rightarrow RCH_2CH(OH)CH_2Cl.$$

The excess of hydrochloric acid was titrated with alkali. The obtained product had m.p. 108.5°.

Found %: C 80.62; H 5.37; N (Kjeldahl) 6.41; epoxyl group 19.21. M 220.8. $C_{15}H_{13}ON$. Calculated %: C 80.68; H 5.87; N 6.28; epoxyl group 19.28. M 223.1.

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SYNTHESIS AND SEPARATION OF DIASTEREOISOMERIC γ-ETHYL-β-AMINOCAPRYLIC ACIDS AND THEIR DERIVATIVES

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N. E. Kozhevnikova was first to synthesize γ-ethyl-β-aminocaprylic acid by the Rodionov reaction [1], employing the condensation of α-ethylhexanal with malonic acid in the presence of alcoholic NH_3, and he described it as a compound with m. p. 186-187° [2].

Since the starting ethylhexanal has a branched chain and already contains an asymmetrical carbon atom, while its conversion into the β-amino acid is accompanied by the appearance of a second asymmetric center, it was natural to expect that two diastereoisomers would be formed:

$$C_4H_9\overset{*}{C}H(C_2H_5)CHO + CH_2(COOH)_2 + NH_3 \rightarrow$$
$$\rightarrow C_4H_9\overset{*}{C}H(C_2H_5)\overset{*}{C}H(NH_2)CH_2COOH.$$

On continuing the work in this direction we were able to actually isolate two diastereoisomers of γ-ethyl-β-aminocaprylic acid and to find a method for their separation. The first isomer (A_1) has m. p. 199-201° (with decomposition); the second isomer (A_2) melts with decomposition at 167°. Isomer A_1 is quite difficultly soluble in water, it crystallizes well and is rapidly precipitated when its solution is cooled; isomer A_2 is more readily soluble, easily gives supersaturated solutions and when recrystallized it deposits from solution only after several hours, and sometimes even after days, crystallizing with a large bulk of solvent. We used the difference in the solubility and in the rate of crystallization to isolate the isomers from the mixture of reaction products. The hydrochloride, and the N-benzoyl-, N-carbethoxy- and N-carbomethoxy- derivatives were obtained for each isomer, and also their amides and esters. For isomer A_1 the ethyl and menthyl esters of the amino acid were obtained, and also the menthyl ester of the benzoyl derivative. By employing the method of fractional crystallization from alcohol and toluene we were able to separate the last compound into two isomers: 1) m. p. 111-112°, $[\alpha]_D^{18}$ −9.64°; 2) m. p. 82-83°, $[\alpha]_D^{18}$ −43°. Saponification of these two isomers gave two benzoyl derivatives, with m. p. 134°, $[\alpha]_D^{18}$ +8.2° and with m. p. 122-123°, $[\alpha]_D^{18}$ −5°. As the melting point values and angles of rotation show, the levorotatory isomer is evidently contaminated with the dextrorotatory isomer.

EXPERIMENTAL

Preparation and isolation of diastereoisomeric γ-ethyl-β-aminocaprylic acids A_1 and A_2. In preparing the amino acids 40 condensations were carried out and each time 20 g of α-ethylhexanal, 16 g malonic acid and 30 ml 8.5% alcoholic ammonia** solution were taken. To the well cooled aldehyde with stirring was gradually added an alcoholic solution of ammonia and then malonic acid was added in small portions. The

*Deceased.

**In carrying out the experiments it was noted that increase of the quantity of reagents lowered the yield.

reaction mass was set aside for 0,5 hour in a freezing mixture and then heated under reflux for 2 hours at 70-80° and for 2 more hours on a boiling water bath. The residues in the flasks (yellow viscous transparent oil) were combined and treated at first with hot water (5 times with 1-liter portions) and then with 12 % HCl (4 times with 700-ml portions). After this treatment, 372 g yellow viscous oil remained which contained unsaturated acid and was not investigated further. From the aqueous extract, evaporated down to 0,25 of initial volume, 125 g of amino acid A_1 came down, m. p. 189°. Further concentration of the aqueous solution yielded a viscous light-yellow syrup, in which, upon addition of concentrated HCl, a solid mass of hydrochlorides of A_1 and A_2 formed. After evaporation of the hydrochloric acid extracts, a mixture of hydrochlorides of amino acids A_1 and A_2 also separated out which was contaminated with traces of unsaturated acid; this was removed by washing the precipitate with ether. To isolate the free amino acid, to the suspension of combined hydrochlorides in 500 ml water was gradually added a 10% solution of NaOH. The precipitate of hydrochlorides dissolved and at pH 7,5 there came down 95 g of amino acid A_1 with m. p. 186-189°. The latter was added to the previously obtained portion of acid A_1 and after two recrystallizations from water, 165 g of amino acid A_1 was isolated with m. p. 199-200° (with decomp.). After isolation of amino acid A_1, there again came down a precipitate from the weakly alkaline filtrate, which was amino acid A_2. It was recrystallized 3 times from water and dried at 100°. Yield 146 g of amino acid A_2 with m. p. 167° (with decomp.) and upon addition of concentrated HCl to the filtrates from recrystallization, 45 g more of its hydrochloride was obtained with m. p. 186-187°. From the remaining filtrates was isolated 174 g more of a mixture of hydrochlorides of amino acids A_1 and A_2. Yield of mixture of isomers was about 50%. The separation yielded 14,1% diastereoisomer A_1, 15,6% diastereoisomer A_2 and 15% unseparated mixture of hydrochlorides of A_1 and A_2. Amino acid A_1 was more difficultly soluble in water than amino acid A_2. It immediately came down upon recrystallization or on solution of the hydrochloride in 10% NaOH and acidification with acetic acid. Its hydrochloride came down upon addition to a solution of concentrated hydrochloric acid.

Amino acid A_2 was readily soluble in water, formed supersaturated solutions and came down very slowly upon recrystallization. When its hydrochloride was dissolved in 10% NaOH and acidified with acetic acid, a precipitate did not come down. The hydrochloride of amino acid A_2 was soluble in water more sparingly than was the hydrochloride of amino acid A_1.

Amino acid A_1. Found %: C 63,94, 63,99; H 11,19, 11,12; N 7,59, 7,44.
Amino acid A_2. Found %: C 64,04, 63,93; H 11,16, 11,14; N 7,23, 7,27. $C_{10}H_{21}O_2N$. Calculated %: C 64,17; H 11,23; N 7,48.

Preparation of hydrochlorides of γ-ethyl- β-aminocaprylic acids A_1 and A_2. When 15 % HCl was added to the amino acid, the resulting solution was transparent and from it almost instantly came down a precipitate of the hydrochloride. It was filtered off, washed with ether and dried at 110°. The hydrochloride of amino acid A_1 was prepared in a yield of 92%, m. p. 192-193°; the hydrochloride of amino acid A_2 was obtained in yield of 86%, m. p. 186-187°. A mixture of the hydrochlorides melted at 175-181°.

Hydrochloride of A_1. Found %: Cl 15,75; N 6,70. Hydrochloride of A_2. Found %: C 53,69, 53,58; H 9,94, 10,06; N 6,38, 6,20; Cl 16,01, 15,88. $C_{10}H_{22}O_2NCl$. Calculated %: C 53,70; H 9,84; N 6,26; Cl 15,88.

Preparation of ethyl esters of γ-ethyl- β-(N-carbomethoxyamino)-caprylic acids A_1 and A_2. The carbomethoxy derivatives were prepared in the usual manner. Yield of carbomethoxy derivative of A_1 was 73,4%, m. p. 75°. Yield of carbomethoxy derivative of A_2 was 67%, m. p. 68,5-70° (from mixture of ethyl and petroleum ethers). A mixture of carbomethoxy derivatives of A_1 and A_2 had m. p. 54-62°. To prepare the esters, the carbomethoxy derivatives were heated for 6 hours with 10 ml of alcohol and 4 ml concentrated H_2SO_4. Yield of ester of carbomethoxy derivative of A_1 was 76%, b. p. 168-170° at 8 mm, m. p. 47°. Yield of ester of carbomethoxy derivative of A_2 was 56,7%, b. p. 174-175° at 9 mm, m. p. 38-39°. A mixture of esters A_1 and A_2 had m. p. 28°.

Ester of A_1. Found %: C 61,77, 61,81; H 10,10, 10,10; N 5,02, 5,03, M 277, 276. Ester of A_2. Found %: C 61,72, 61,89; H 9,60, 9,77; N 5,18, 5,09, M 271, 274. $C_{14}H_{27}O_4N$. Calculated %: C 61,53; H 9,89; N 5,12, M 273.

Preparation of benzoyl derivatives of γ-ethyl-β-aminocaprylic acids A_1 and A_2. To the cooled solution of amino acid in 10% solution (3 moles of alkali per 1 mole of acid) was added drop-wise benzoyl chloride. The precipitate obtained upon acidification was boiled 3 times with water and recrystallized from aqueous solution; the melting point of the derivative of isomer A_1 was 132°; the melting point of the derivative of isomer A_2 was 121° (from aqueous alcohol). Yield 80-85%.

Derivative of isomer A_1. Found %: C 70.31, 70.18; H 8.72, 8.91; N 4.93, 4.99. Derivative of isomer A_2. Found %: C 70.14, 69.99; H 8.52, 8.68; N 5.05, 5.25. $C_{17}H_{25}O_3N$. Calculated %: C 70.10; H 8.52; N 4.81.

Preparation of amides of benzoyl derivatives of γ-ethyl-β-aminocaprylic acids A_1 and A_2. 5 g of benzoyl derivative, 1.25 ml $SOCl_2$ and 10 ml dry benzene were heated at 40° for 3-4 hours and then 300 ml absolute ether was added and the solution was saturated with NH_3 upon cooling. The precipitate was washed with 5% NaOH solution, water, and recrystallized from 90-95% methyl alcohol. The derivative of A_1 had m. p. 174-175° (long colorless needles), yield 76%. The derivative of A_2 had m. p. 184-185° (colorless needles), yield 70%. The mixture of isomers had m. p. 168-170°.

Derivative of A_1. Found %: C 70.24, 70.47; H 8.58, 8.74; N 9.81, 9.75. Derivative of A_2. Found %: C 70.39, 70.69; H 8.58, 8.70; N 9.65, 9.76. $C_{17}H_{26}O_2N_2$. Calculated %: C 70.34; H 8.96; N 9.62.

Preparation of ethyl ester of γ-ethyl-β-aminocaprylic acid A_1. 5 g amino acid, 50 ml ethyl alcohol and 4 ml concentrated H_2SO_4 were heated for 8 hours on a water bath. The excess of alcohol was driven off, the residue was diluted with water, the alkalized extract was washed with 5% $NaHCO_3$ solution, water, and dried with $NaSO_4$. The ether was driven off and the residue was vacuum-distilled. Yield 3.8 g (66%), b. p. 121-122° at 4 mm.

Found %: C 67.54; H 11.68; N 6.36, 6.29. $C_{12}H_{25}O_2N$. Calculated %: C 67.00; H 11.63; N 6.51.

On treatment in the cold with a 5% solution of NaOH, the ester immediately was hydrolyzed to the amino acid. On standing, it slowly decomposed with evolution of NH_3 and formation of an ester of an unsaturated acid.

Preparation of menthyl ester of γ-ethyl-β-aminocaprylic acid A_1. 5 g of amino acid and 2.2 ml $SOCl_2$ were heated for 2 hours at 40-43° and then 200 ml absolute ether was added and, drop-wise with cooling and stirring, 4.2 g menthol in 50 ml absolute ether was added. The precipitate of hydrochloride which separated out was washed with ether, treated with $NaHCO_3$ solution and extracted with ether. Yield 4.4 g menthyl ester with b. p. 189-190° at 5 mm.

Found %: C 73.63, 73.65; H 12.33, 12.50; N 4.67, 4.57. $C_{20}H_{39}O_2N$. Calculated %: C 73.84; H 12.00; N 4.30.

An attempt to separate the optically active isomers by fractionation of the menthyl ester with a column at 3 mm resulted in its decomposition with evolution of NH_3 and formation of unsaturated acid. On addition of 17% HCl to the ester, its hydrochloride was obtained with m. p. 138-139°.

Preparation of menthyl ester of γ-ethyl-β-(N-benzoylamino)-caprylic acid A_1. 15 g of benzoyl derivative was heated at 40° with 3.75 ml $SOCl_2$ at first without solvent and then 200 ml absolute ether was added and heating was continued for 4 hours more at the boiling point of the solution. Ether and excess $SOCl_2$ were driven off in the cold in vacuum; to the residue was added 200 ml absolute ether, and, with cooling, 10 g menthol in 100 ml absolute ether was added drop-wise. The latter was distilled off and the unreacted menthol was driven off with steam. The remaining oil was dissolved in ether, the ethereal solution was washed with 5% NaOH solution, water, and dried with sulfate. After driving off the solvent, 18.1 g of menthyl ester was obtained. Upon crystallization first from toluene and then from aqueous alcohol (or ether), two isomers were isolated: one with m. p. 111-112° (4.7 g) $[\alpha]_D^{18}$ −9.64° (16.66% solution in alcohol) and one with m. p. 82,83° (5.6 g); $[\alpha]_D^{18}$ −43° (15% solution in alcohol); also 6 g of mixture remained with m. p. 76-101°. The mixture of isolated isomers had m. p. 76-79°.

Isomer with m. p. 111-112°. Found %: C 76.03, 75.87; H 9.50, 9.51; N 3.69, 3.54. Isomer with m. p. 82-83°. Found %: C 75.58, 75.74; H 10.40, 10.29; N 3.80, 3.87. $C_{17}H_{25}O_3N$. Calculated %: C 75.70; H 9.81; N 3.49.

Saponification of 3 g of ester with m. p. 111-112° with NaOH solution yielded 1,85 g of benzene derivative with m. p. 133-134°; $[\alpha]_D^{18}$ +8,2° (10% solution in alcohol).

Saponification of 3 g of ester with m. p. 82-83° yielded 1,92 g of benzene derivative with m. p. 122-123°; $[\alpha]_D^{18}$ -8,5° (10% solution in alcohol).

SUMMARY

Two diastereoisomers (A_1 and A_2) of γ-ethyl-β-aminocaprylic acid were obtained, and also their hydrochlorides, N-acyl derivatives, amides and esters.

The fractional crystallization of the menthyl ester of γ-ethyl-β-(N-benzoylamino) caprylic acid A_1 gave two isomers, the saponification of which yielded two optically active forms of γ-ethyl-β-(N-benzoylamino) caprylic acid.

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[2] N. E. Kozhevnikova, Dissertation: "Synthesis of γ-Ethyl-β-Aminocaprylic and β-Aminocaprylic Acids and a Study of Some of Their Reactions", Moscow (1952).

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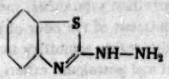
SYNTHESIS OF THIAZOLE DERIVATIVES

XI. SOME NEW HYDRAZINES OF THE BENZOTHIAZOLE SERIES

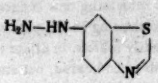
V. M. Zubarovsky

Of the antitubercular compounds known at the present time the hydrazides of heterocyclic acids and the thiosemicarbazones of aromatic and heterocyclic aldehydes show the greatest activity. The structure of these compounds permits regarding them as hydrazine derivatives. In any case their antitubercular activity is definitely associated with the presence of the elements of the hydrazine structure in their molecules. From this viewpoint the synthesis of hydrazines of the heterocyclic series and a study of their antitubercular properties deserve attention.

The hydrazines of the benzothiazole series were the subject of the present study. The derivatives of 2-benzothiazolylhydrazine (I) appear as known hydrazines of this series. 6-Benzothiazolylhydrazine (II) has also been synthesized, but none of its substituted derivatives have been prepared.



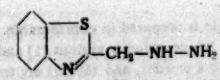
(I)



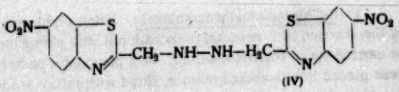
(II)

Other benzothiazolylhydrazines with the hydrazino group found in various positions in the benzene ring of benzothiazole or in the side chain are unknown. In this communication we describe the synthesis of several new benzothiazolylhydrazines.

We described 2-bromomethylbenzothiazole [1] and 2-chloromethylbenzothiazole [2] in previous studies. Both of these halide derivatives can serve as starting products for the synthesis of 2-benzothiazolylmethylhydrazine (III):



(III)

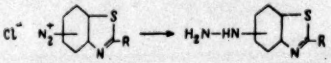


(IV)

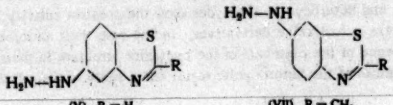
However, it is more convenient to use the more readily available 2-chloromethylbenzothiazole, in the synthesis of which we have now introduced changes, permitting its immediate preparation in large amounts. The heating of 2-chloromethylbenzothiazole with hydrazine hydrate in alcohol medium yields hydrazine (III). Under similar conditions 2-chloromethyl-6-nitrobenzothiazole, in which the chlorine atom shows a more labile character,

yields the disubstituted symmetrical bis (6-nitro-2-benzothiazolylmethyl) hydrazine (IV).

The various 5- and 6-hydrazinobenzothiazoles were synthesized by a general method – the reduction of 5-benzothiazolyl- and 6-benzothiazolyldiazonium chlorides with stannous chloride:



The benzothiazolylhydrazines (V-IX) were obtained by the same method:



(V) R = H
(VI) R = CH_3

(VII) R = CH_3
(VIII) R = CH_2OH
(IX) R = SCH_3

The symmetrical disubstituted hydrazine (IV) is a high melting yellow substance, insoluble in most organic liquids. All of the remaining new benzothiazolylhydrazines are colorless crystalline substances, melting without decomposition, and showing in the pure state a hardly perceptible odor, reminiscent of the odor of phenylhydrazine; all of them are readily soluble in dilute mineral and organic acids, show considerable solubility in water and in most organic liquids when heated, but are insoluble or poorly soluble in ethyl and petroleum ethers. The benzothiazolylhydrazines, characterized by a greater solubility in water, reduce Fehling reagent in the cold, and the others – when heated.

With acetic anhydride the benzothiazolylhydrazines yield monoacetyl derivatives, and with benzaldehyde – the benzothiazolyl-substituted hydrazones of benzaldehyde.

The benzothiazolylhydrazines with the hydrazino group in the benzene ring are substances that are easily oxidized and altered. When stored they turn dark and acquire the odor of benzothiazole or of the alkylbenzothiazoles; their acetyl derivatives and hydrazones show complete stability. 2-Benzothiazolylmethylhydrazine fails to show change when stored.

The antitubercular activity of the new benzothiazolylhydrazines proved to be low.

EXPERIMENTAL

1. 2-Chloromethylbenzothiazole. When 2-chloromethylbenzothiazole is prepared in considerable quantity by the reaction of 2-benzothiazolylcarbinol with phosphorus pentachloride, this reaction is violent [1] and must be carried out in toluene medium. 42 g phosphorus pentachloride, rubbed to a powder, and 150 ml dry toluene were placed in a 3-necked reactor, fitted with reflux condenser, stirrer and thermometer, and to the suspension was immediately added 30.0 g 2-benzothiazolylcarbinol. Upon stirring, the mixture of reagents heated up due to the exothermal reaction and became liquid. When the temperature began to fall, the mixture was heated, and stirring was continued until the mixture started to boil; boiling was continued for 15 minutes until a light-brown solution formed. Heating was stopped and the hardening mass was stirred for 30 minutes more and then pieces of ice and 20% aqueous soda solution was added until the reaction was alkaline. The reaction mass was carefully stirred and the toluene layer was separated. The aqueous layer was extracted three times with toluene

(25 ml each time). The toluene solution was dried with calcium chloride and filtered. After driving off the toluene, the residue was distilled under the vacuum of a water-jet pump and the fraction was collected with b. p. 130-142° at 7-10 mm. Yield of colorless oily liquid 20.0 g (60.5%). It was vacuum-distilled and 18 g of pure product was obtained, b. p. 121-122° at 4 and 145° at 12 mm. The substance crystallized even during the distillation.

2. 2-Benzothiazolylmethylhydrazine (III). To 5.6 g 2-chloromethylbenzothiazole was added 2 ml alcohol and 6.0 g hydrazine hydrate. The layered mixture was shaken for 15 minutes and slowly warmed up and then it was boiled for 2.5 hours and was poured into 59 ml water with ice. Upon stirring and cooling, the yellow reaction product became semisolid. It was filtered off and carefully rubbed in a mortar with petroleum ether, the latter being changed several times (4-5 times, 25-ml portions). The hydrazine, freed from yellow oily admixtures, was filtered off and washed with petroleum ether. Yield 2.3 g (42.8%).

The crude hydrazine was crystallized (using charcoal) from 300 ml ligroine (b. p. 100-120°) and after cooling the mother liquor with ice, 1.5 g of hydrazine was obtained in the form of yellowish-white needles with m. p. 130°. After two more crystallizations (with charcoal) with ligroine, the hydrazine was in the form of colorless needles with m. p. 135° (corr.).

Found %: N 23.62, 23.71. $C_9H_9N_3S$. Calculated %: N 23.46.

Acetyl derivative. 0.54 g 2-benzothiazolylmethylhydrazine was dissolved with heating in 75 ml ligroine; into the boiling solution was immediately run 11 ml of warm ligroine solution of 0.4 g acetic anhydride and the mixture was boiled for 10 minutes. Even during boiling, a crystalline precipitate started to form. The suspension was set aside to cool for 1 hour and then the precipitate was filtered off and washed with methanol. Yield 0.6 g (90.5%). The acetyl derivative was recrystallized twice from a 20-fold quantity of isobutyl alcohol (with charcoal) and was obtained in the form of colorless needles with m. p. 216° (corr.).

Found %: N 18.74. $C_{10}H_{11}ON_3S$. Calculated %: N 19.00.

2-Benzothiazolylmethylhydrazone of benzaldehyde. Into the hot aqueous solution of hydrazine (III) was run a hot solution of benzaldehyde in methanol with stirring. Equimolar quantities of reagents were used. A precipitate immediately separated out which was filtered off from the still warm solution, washed with water and recrystallized from a considerable quantity of ethyl alcohol. After two crystallizations, pale-yellow crystals were obtained with m. p. 158° (corr.).

3. Symmetrical bis-(6-nitro-2-benzothiazolylmethyl) hydrazine (IV). To 2.3 g 6-nitro-2-chloromethylbenzothiazole was added a solution of 2.0 g hydrazine hydrate in 2 ml ethyl alcohol. When the exothermal reaction was complete, the mixture was heated for 30 minutes at 100° and after cooling, was poured in water. The reddish light-brown precipitate was filtered off and washed with water, warm methanol and ether. Yield 1.57 g (75%). The substance was virtually insoluble in most organic solvents. It was recrystallized twice from a large quantity of acetophenone and charcoal was used during the first crystallization. Orange-yellow fine crystals were obtained with decomposition point 320° in sealed capillary.

Found %: N 19.80. $C_{16}H_{12}O_4N_6S_2$. Calculated %: N 20.19.

4. 5-Benzothiazolylhydrazine (V). 5-Aminobenzothiazole, necessary for the synthesis of hydrazine (V), was prepared by reduction of 5-nitrobenzothiazole. Reduction of the latter was carried out by Spieler and Priis [3] who prepared the double stannic and hydrochloride salts of 5-aminobenzothiazole and its acetyl derivative but did not describe the free base. The acetyl derivative of 5-aminobenzothiazole was synthesized previously by Peticola and coworkers [4], which also did not isolate 5-aminobenzothiazole. We prepared 5-aminobenzothiazole by the method of Spieler and Priis in the form of the double stannic salt and from this we isolated the base by the usual method. The salt was dissolved with mild heating in a 10-fold quantity of water and to the filtered solution was added 20% caustic soda solution until solution of stannic hydroxide. The white precipitate of 5-aminobenzothiazole was filtered off and washed with a small quantity of cooled water. Yield of amine 73.3%, m. p. 78° (corr.). Upon brief boiling of a concentrated benzene solution of equal weights 5-aminobenzothiazole and acetic anhydride, the acetyl derivative formed, which after crystallization from alcohol (with charcoal), was in the form of colorless crystals with m. p. 194° (corr.), 188-189° [3], 191-192° [4].

1.5 g of 5-aminobenzothiazole was dissolved in 6 ml dilute (1:1) hydrochloric acid and diazotized with 0.95 g of sodium nitrite, dissolved in 3 ml water at −3° to 0°. A turbid slightly frothy pink solution formed, which gradually, though rapidly if possible, at a temperature not exceeding +8° with stirring, was added to a solution of 5.25 g stannic chloride in 6 ml concentrated hydrochloric acid. The mixture was heated for 30 minutes at 100°. To the cooled mixture was added ice (an excess of ice must be avoided since 5-hydrazinobenzothiazole is rather soluble in water), and then a 20% aqueous solution of caustic soda until solution of stannic hydroxide, which separated out upon neutralization, with a slight excess. The precipitate of hydrazine was filtered off and recrystallized (using charcoal) from 15 ml water. Yield after one crystallization 0.85 g (51.5%), m. p. 90-91°. Upon crystallization from a large quantity of ligroine, colorless needles were obtained, which turned pink upon mild heating or simply upon passage of time; the odor of benzothiazole also became perceptible. Washing of the hydrazine with petroleum ether, in which it was soluble, liberated it from benzothiazole. The hydrazine was sparingly soluble in ethyl ether.

Evidently, due to readily occurring alteration of the hydrazine, the determination of nitrogen in it led to low figures: 23.70 instead of 25.45%, calculated for $C_7H_7N_3S$. Therefore, from the hydrazine and benzaldehyde we prepared the hydrazone, which was analyzed.

5-Benzothiazolylhydrazone of benzaldehyde. 0.17 g hydrazine, 5 ml methyl alcohol, 1 ml glacial acetic acid and 0.5 ml benzaldehyde were heated to the boil in the course of 5 minutes. To the hot solution was added 5 ml water, the yellowish-white crystals of the hydrazone which came down were filtered off, washed with cooled methanol and twice recrystallized from ethyl alcohol (with charcoal). Yellowish-white flakes, m. p. 175° (corr.).

Found %: N 16.65, 16.83. $C_{14}H_{11}N_3S$. Calculated %: N 16.60.

5. 2-Methyl-5-benzothiazolylhydrazine (VI). 2-Methyl-5-nitrobenzothiazole was prepared by the method which we published previously [5] and was reduced to the corresponding amine by means of tin and hydrochloric acid. To synthesize hydrazine (VI) we used 8.2 g 2-methyl-5-aminobenzothiazole in 30 ml dilute (1:1) hydrochloric acid, 3.6 g sodium nitrite, dissolved in 15 ml water, and a solution of 27.5 g stannous chloride in 29 ml concentrated hydrochloric acid. The method of synthesis differed slightly in detail from the method used in synthesizing hydrazine (V).

Diazotization was carried out at 0°. The transparent cooled solution of diazonium salt was added dropwise to a solution of stannous chloride in hydrochloric acid at such a rate that the temperature of the mixture stayed between 0 and +5°. On completion of addition, cooling was stopped and the mixture was stirred for 30 minutes and then was heated at 100° for 30 minutes, again cooled, mixed with ice (200 g) and treated with 20% aqueous solution of caustic soda (225 ml). The yellow precipitate of hydrazine was filtered off and carefully washed with water. The moist crude hydrazine had to be immediately purified; the hydrazine was dissolved in 50 ml dilute (1:2) hydrochloric acid, the solution was heated to 50° and decolorized three times (with charcoal, 1.5, 1.0 and 1.0 g portions) and then was shaken with charcoal 3 minutes each time. To the decolorized solution was added ice and ammonia. The white crystalline precipitate of hydrazine was filtered off and washed with water. Yield of purified hydrazine (VI) 4.1 g (45.8%). After crystallization (with charcoal) from a 12-fold quantity of methyl alcohol, the hydrazine was in the form of colorless needles, m. p. 159° (corr.). For analysis, the hydrazine was again washed with ether (in which it was quite soluble), dried in vacuum at 75° for 15 minutes and immediately analyzed.

Found %: N 23.58, 23.28. $C_8H_9N_3S$. Calculated %: N 23.46.

Multiple crystallizations from methyl alcohol yielded hydrazine with m. p. 161° (corr.).

Acetyl derivative. 1.8 g of 2-methyl-5-benzothiazolylhydrazine was rapidly stirred with 2.5 ml acetic anhydride. In a short time a transparent solution formed, which instantly warmed up and was converted to a solid mass. 20 ml water was added, the acetyl derivative was filtered off, washed with water and recrystallized from a 10-fold quantity of dilute (1:2) alcohol charcoal was used. Yield 1.33 g (60%). After two crystallizations, colorless needles were obtained, m. p. 188° (not sharp).

2-Methyl-5-benzothiazolylhydrazone of benzaldehyde. 0.36 g hydrazine was mixed with 0.5 ml benzaldehyde. The mass was heated at 100° for 15 minutes and the crude hydrazone was twice crystallized (with charcoal) from methyl alcohol. Yield 0.3 g, m. p. 160°. Due to the agreement of the melting points of the hydrazone and hydrazine, from which it was obtained, the melting point of the mixture of the two substances was obtained, it was 132-137°.

6. 2-Methyl-6-benzothiazolylhydrazine (VII). Taken for synthesis of hydrazine (VII): 9.84 g 2-methyl--6-aminobenzothiazole, dissolved in 35 ml 20% hydrochloric acid, a solution of 4.3 g sodium nitrite in 20 ml water and a solution of 33.8 g stannous chloride in 35 ml concentrated hydrochloric acid. The method of synthesis and purification of the hydrazine was the same as described in Experiment 5. Yield of impure hydrazine (VII) 8.0 g (73.2%), m. p. 145°. After two more crystallizations from methyl alcohol, colorless needles were obtained with m. p. 149° (corr.).

Found %: N 23.59, 23.68. $C_8H_9N_3S$. Calculated %: N 23.46.

Acetyl derivative of hydrazine (VII) was prepared in yield of 70% in the same manner as for the preparation of the acetyl derivative of hydrazine (VI) (Experiment 5). After four crystallizations from dilute alcohol, colorless crystals were obtained with m. p. 205° (corr.).

Found %: S 14.42, 14.37. $C_{10}H_{11}ON_3S$. Calculated %: S 14.48.

2-Methyl-6-benzothiazolylhydrazone of benzaldehyde was prepared from equimolar quantities of hydrazine and benzaldehyde. Benzaldehyde was added to the hydrazine, dissolved in a 3-fold quantity of alcohol and the mixture was boiled. The hydrazone that separated out was obtained after four crystallizations from toluene (with charcoal) in the form of fine yellowish crystals with m. p. 203° (corr.).

7. 2-Hydroxymethyl-6-benzothiazolylhydrazine (VIII). Taken for preparation of hydrazine (VIII): 1.8 g 6-amino-2-benzothiazolylcarbinol [6] dissolved in 12 ml dilute (1:1) hydrochloric acid, 0.83 g sodium nitrite dissolved in 6 ml water, and a solution of 7.0 g stannic chloride in 8 ml concentrated hydrochloric acid. The method of synthesis of hydrazine (V) was used. The yellowish-white precipitate of crude hydrazine was filtered off and washed with a 2% aqueous solution of caustic soda and water. The hydrazine was recrystallized three times from methyl alcohol (with charcoal)– colorless needles were obtained with m. p. 150° (corr.). The mixture of hydrazine with 6-amino-2-benzothiazolylcarbinol (m. p. 151°) had m. p. 113°. Analysis of the hydrazine for nitrogen gave low figures and, therefore, the hydrazone was analyzed.

2-Hydroxymethyl-6-benzothiazolylhydrazone of benzaldehyde formed when a mixture of 0.59 g of hydrazine (VIII), 0.5 ml benzaldehyde, 0.5 ml glacial acetic acid and 8 ml methyl alcohol was boiled for 20 minutes. The hydrazone came down even during boiling. Yield 0.65 g. After three crystallizations from ethyl alcohol (with charcoal), the obtained hydrazone had m. p. 200° (corr.).

Found %: S 11.39, 11.41. $C_{15}H_{13}ON_3S$. Calculated %: S 11.31.

8. 2-Methylmercapto-6-benzothiazolylhydrazine (IX). Taken for synthesis: 3.92 g 2-methylmercapto--6-aminobenzothiazole, which was dissolved in 24 ml dilute (1:1) hydrochloric acid, a solution of 1.66 g sodium nitrite in 12 ml water and a solution of 13.6 stannous chloride in 14 ml concentrated hydrochloric acid. The method of synthesis and purification of the hydrazine was the same as described for Experiments 5 and 6 with the difference that after pouring the diazo solution into the solution of stannous chloride, the mixture was placed in boiling water for 10 minutes in all and then the clump of resin that had formed toward completion of heating was removed from the transparent solution and the hydrazine separated out from the latter. Yield of impure air-dried hydrazine 3.0 g (71%). After one crystallization from a 15-fold quantity of ethyl alcohol, the hydrazine was obtained in the form of white fine needles with m. p. 115° (corr.).

Found %: N 19.92, 20.14. $C_8H_9N_3S_2$. Calculated %: N 19.90.

Upon being dried in air in the light, the hydrazine turned pink on the surface due to its sparing solubility in water, it reduced Fehling solution only upon heating.

Acetyl derivative. 0.53 g of 2-methylmercapto-6-benzothiazolylhydrazine, purified by precipitation with ammonia from a solution of its hydrochloride, was mixed with 2 ml water and to the resulting slurry was immediately added acetic anhydride (2.5 g) with vigorous mixing. A solution formed, from which a crystalline precipitate immediately separated out. After 5 minutes, an excess of water was added and the acetyl derivative was filtered off. After 2 crystallizations (with charcoal) from dilute (1:2) ethyl alcohol, colorless lustrous crystals were obtained with m. p. 190-192° (corr.).

Found %: N 16.56, 16.68. $C_{10}H_{11}ON_3S_2$. Calculated %: N 16.60.

2-Methylmercapto-6-benzothiazolylhydrazone of benzaldehyde was prepared by boiling a mixture of 1.05 g hydrazine (IX), 20 ml ethyl alcohol, 5 ml glacial acetic acid and 0.8 g benzaldehyde for 30 minutes. The solution was cooled and the hydrazone was precipitated by addition of an excess of water. The crude hydrazone was treated with 10 ml dilute (1:50) hydrochloric acid to remove possible admixture of hydrazine. Yield 0.75 g (50.4%). After 2 crystallizations (with charcoal) from ethyl alcohol, lustrous yellow crystals were obtained with m. p. 149° (corr.).

Found %: N 13.80; S 21.45. $C_{15}H_{13}N_3S_2$. Calculated %: N 14.04; S 21.40.

SUMMARY

Some new hydrazines of the benzothiazole series were synthesized. Treatment of 2-chloromethylbenzothiazole and 6-nitro-2-chloromethylbenzothiazole with hydrazine hydrate gave 2-benzothiazolylmethylhydrazine and bis(6-nitro-2-benzothiazolylmethyl)hydrazine, respectively. Diazotization of the benzothiazolylamines, followed by reduction of the diazonium salts with stannous chloride gave 5-benzothiazolyl-, 2-methyl-5-benzothiazolyl-, 2-methyl-6-benzothiazolyl-, 2-hydroxymethyl-6-benzothiazolyl- and 2-methylmercapto-6-benzothiazolylhydrazines.

The properties of these hydrazines were described and their derivatives were prepared.

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CATALYTIC AMINATION OF ORGANIC COMPOUNDS

IV. CATALYTIC AMINATION OF NITRO COMPOUNDS OF THE AROMATIC SERIES

N.S. Kozlov and G.N. Kozlov

The unsuccessful attempts made to introduce mononitro compounds of the aromatic series into reaction with ammonia have created the essentially incorrect assumption in contemporary organic chemistry that it is impossible to replace the nitro group in these compounds by the amino group. Assumptions of this nature found expression in the work of A.G. Horst [1], in which the author, summarizing the experimental facts known up to then, wrote: "nitrobenzene fails to react under heating with either ammonia or with sodium alcoholate". This observation refers not only to nitrobenzene, but also to the mononitro derivatives of benzene homologs and the mononitro derivatives of naphthalene. Also a halogen atom, attached to a carbon atom of the benzene ring, is chemically extremely passive and unreactive. Only under special conditions – elevated temperature, high pressure, and in the presence of suitable catalysts – will chlorobenzene, for example, react with ammonia, being transformed into aniline [2].

As is known, A.N. Engelhardt and P.A. Lachinov [3] were the first to establish that the chlorine found in aromatic chloronitro compounds becomes reactive under the influence of the nitro group and is capable of being replaced by the amino group. Here it is timely to mention that this is characteristic only for the o- and p-chloronitrobenzenes. In m-nitrochlorobenzene this chlorine atom shows the same inertness as in chlorobenzene itself: m-chloronitrobenzene fails to react with ammonia, even at elevated temperature [4]. But in the work of N.N. Vorozhtsov and V.A. Kobelev [5] it was shown that the reaction of m-chloronitrobenzene with ammonia in the presence of cuprous chloride as catalyst can yield m-nitroaniline. Consequently, in the reaction of o-, m- or p-chloronitrobenzene with ammonia the chlorine atom enters into the reaction, while the nitro group remains unchanged.

Aromatic di- and polynitro compounds, having a greater number of nitro groups, show an increase in their activity and in their capacity for substitution reactions. Thus, the o- and p-nitroanilines can be obtained by the reaction of ammonia with the o- and p-dinitrobenzenes, respectively [6]. It is also interesting to mention that attempts to replace the nitro group in m-dinitrobenzene by the amino group have been unsuccessful [4]. Consequently, here also definite rules are observed relative to the influence shown by substituents in the benzene ring on the chemical properties of other substituents.

In the present work we studied the catalytic amination of aromatic mononitro compounds. We used activated aluminum oxide as the catalyst, which, as is known, proved to be an extremely active catalyst in the replacement of the hydroxyl group in phenols by the amino group [7,8]. Since in our case there was hardly any reaction with ammonia at atmospheric pressure, we introduced ammonia compressed to 7-9 atmospheres into the reaction. The experiments were run in a flow system apparatus, which was described earlier [7]. Our experiments revealed that under the investigated conditions it is possible to replace the nitro group in mononitro derivatives of aromatic compounds by the amine group. We obtained aniline from nitrobenzene, and o- and p-toluidine from o- and p-nitrotoluene, respectively.

The presence of ammonium nitrate in the reaction products gives basis to express the end result of these reactions by the following equation:

$$RNO_2 + NH_3 = R - NH_2 + HNO_2 \xrightarrow{NH_3} NH_4NO_2.$$

In the experiments on the amination of the o- and m-chloronitrobenzenes under the investigated conditions it was established that these compounds are converted into the o- and m-chloroanilines. Consequently, in contrast to the generally accepted theories on the mobility of the chlorine atom found in chloronitro derivatives of benzene, under our studied conditions the amino group replaces the nitro group, and not the chlorine atom. But we believe that the possibility of replacing the chlorine atom found in chloronitrobenzenes by the amino group is not excluded, since the nitroanilines and diamines that are formed when the reaction proceeds in this manner show decomposition at elevated temperature. It is entirely possible that some of the aniline found in our experiments was formed as the result of decomposition.

EXPERIMENTAL

Experiment 1. 20 g nitrobenzene was passed at the rate of 20 drops per minute at atmospheric pressure in a stream of ammonia over aluminum oxide, heated to 370°. Yield 19 g of homogeneous product, which proved to be virtually unchanged nitrobenzene. The presence of aniline in the product could be only analytically detected. Consequently, under these conditions, replacement of the nitro group by the amino group did not take place.

Experiment 2. 20 g nitrobenzene was aminated but in contrast to the preceding experiment, the ammonia pressure during the experiment was equal to 8 atmospheres. Yield 19 g catalyzate, which consisted of two layers – a lower oily layer, which consisted of the main mass of the catalyzate and an upper aqueous layer. The catalyzate was treated with HCl (1:3). From the neutral portion was separated 11 g unchanged nitrobenzene and from the acid portion, after alkalization, was isolated 5 g amine, which distilled in the range 180-182°. This product proved to be pure aniline: n_D^{20} 1.6874, d_4^{20} 1.023. From it was prepared acetanilide with m.p. 113°. Yield of aniline was 33%, on taken and 71%, on reacted nitrobenzene.

When amination of 20 g nitrobenzene was carried out under these conditions but at a rate of 10 drops per minute, 7 g nitrobenzene and 7.5 g aniline (50%, on taken or 88.1% on reacted nitrobenzene) were obtained.

Experiment 3. Amination of 20 g o-nitrotoluene was carried out under the conditions of the preceding experiment. The rate of introduction of substance on the catalyst was 15 drops per minute. From the catalyzate was isolated 9 g unchanged o-nitrotoluene and 4 g o-toluidine (25.5%, on taken or 46.5% on reacted o-nitrotoluene). Resinification of the catalyst was noted.

Experiment 4. Amination of 20 g p-nitrotoluene was carried out under the same conditions as those of the preceding experiment. From the catalyzate was isolated 10 g unchanged p-nitrotoluene and 5 g p-toluidine with m.p. 43°, and an acetyl derivative with m.p. 152°. Yield of p-toluidine 35.4%, on taken or 70.5% on reacted p-nitrotoluene.

Experiment 5. Amination of 20 g o-chloronitrobenzene was carried out under the conditions of the preceding experiment. From the catalyzate was isolated 6 g unchanged o-chloronitrobenzene and 3.5 g amines, which distilled in the range 195-210°. The weight of the catalyst increased by 6 g. The amines obtained from three experiments were distilled; fractions were separated with b.p. 180-182° (0.5 g) and 206-208° (6 g). The 1st fraction proved to be aniline, which was confirmed by preparation of acetanilide. The product with b.p. 206-208° had the following constants: d_4^{20} 1.225, n_D^{20} 1.5818; it proved to be o-chloroaniline.

Amination of 20 g m-chloronitrobenzene was carried out under the same conditions. From the amination products was isolated 6 g unchanged m-chloronitrobenzene and 4 g amines; the latter distilled in the range 205-230°. A fraction was separated with b.p. 225-230° (2.5 g), d_4^{20} 1.225, n_D^{20} 1.5890. This product was m-chloroaniline.

α-Nitronaphthalene was aminated under the same conditions but the yield of *α*-naphthylamine was quite negligible, about 1 g per 20 g *α*-nitronaphthalene taken for reaction. A strong resinification of the catalyst was observed. Upon amination of m-dinitrobenzene, there was marked decomposition of the products and a small amount of m-nitroaniline was separated.

It is important to note that after completion of each experiment, a deposit of crystals of inorganic substance was noted in the lower part of the reaction tube; it proved to be ammonium nitrite.

SUMMARY

The catalytic amination of mononitro derivatives of aromatic hydrocarbons with ammonia compressed to

9 atm. was studied in the presence of activated aluminum oxide. It was established that the reaction of ammonia with nitrobenzene yields aniline, with o- and p-nitrotoluenes – the o- and p-toluidines, and with o- and m-chloronitrobenzenes – the o- and m- chloroanilines. As a result, a new method was discovered for replacement of the nitro group by the amino group.

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placement of the nitro group by the amino group.

and m-chloronitrobenzene – the o- and m- chloroanilines. As a result, a new method was discovered for replacing with nitrobenzene yields aniline, with o- and p-nitrotoluenes - the o- and p-toluidines, and with o-

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THE PREPARATION OF ARYLSULFONYL DERIVATIVES OF AMINO ACIDS*

L.N. Nikolenko

In connection with studying the reaction of arylsulfonylglycines with ammonia it became necessary for us to synthesize some members of this group of compounds.

As is known, the arylsulfonylamino acids can be obtained by three methods: reaction of the arylsulfonyl chloride with amino acids [1,2], saponification of the nitriles of arylsulfonylamino acids [3,4], and alkylation of the sulfonamides of halocarboxylic acids [5,6].

We established that alkylation of the arylsulfonamides of monochloroacetic acid in the presence of calcium hydroxide is a convenient method for the synthesis of arylsulfonylglycines (Method Ia). As a rule, the yields are satisfactory. In individual cases we obtained the arylsulfonyl derivatives of amino acids by other methods, described in the literature: alkylation of the arylsulfonamides of monochloroacetic acid in the presence of sodium hydroxide (Method 1b) and by the method of E. Fischer and M. Bergmann (Method II) [7].

EXPERIMENTAL

Experiment 1. A mixture of 100 g 4-toluenesulfonamide (m.p. 134-136°), 28 g calcium oxide and a solution of 53 g sodium monochloroacetate in 500 ml water was heated on a boiling water bath for 16 hours in a flask fitted with reflux condenser and stirrer.

After separation of unreacted amide and calcium hydroxide, 4-toluenesulfonylglycine was separated out by acidification of the filtrate with hydrochloric acid. The precipitate was separated off, washed with water and dried in the air.

Experiment 2. To a solution (heated to 95-97°) of 50 g phenylglycine in 100 ml 15% soda solution was at first added 110 g 4-toluenesulfochloride and then 200 ml 10% caustic soda solution drop-wise in the course of 2 hours. After stirring for 4 hours at the given temperature, the reaction mass was cooled to room temperature and 4- toluenesulfonyl-N-phenylglycine was separated out by acidification of the reaction mass with hydrochloric acid.

The experimental results on the synthesis of other arylsulfonyl-substituted amino acids are given in the table.

SUMMARY

Twenty-three arylsulfonyl derivatives of amino acids were synthesized, of which 17 are new.

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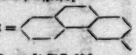
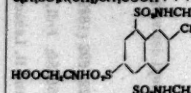
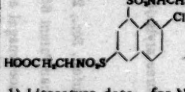
	Formula	Method of preparation	Yield (in %)	External appearance	Melting point	Analysis for nitrogen (%) found	Analysis for nitrogen (%) calc.
	RSO_2NHCH_2COOH						
1	$R = C_6H_5$	Ia	80	Colorless needles	165—165.5°	—	—
2	$R = 2\text{-}CH_3C_6H_4$	Ia	40	Ditto	142.5—143	6.45	6.11
3	$R = 2,4\text{-}(CH_3)_2C_6H_3$	Ia	73	" "	110—111	5.71, 5.71	5.76
4	$R = 2,4,6\text{-}(CH_3)_3C_6H_2$	Ia	42	" "	156.5—157	5.74, 5.98	5.44
5	$R = 4\text{-}CH_3C_6H_4$	Ia	90	" "	148—149	—	—
6	$R = 4\text{-}CH_3OC_6H_4$	Ia	22	" "	129	5.75, 5.86	5.71
7	$R = 4\text{-}CH_3CONHC_6H_4$	Ia	58	White powder	230	10.63, 10.65	10.29
8	$R = 4\text{-}ClC_6H_4$	Ia	61	Long needles	176—176.3	5.91, 5.84	5.61
9	$R = 3\text{-}NO_2C_6H_4$	Ia	56	Yellow needles	148—149	—	—
10	$R = \alpha\text{-}C_{10}H_7$	Ia	10.5	White powder	145.5	5.23, 5.31	5.28
11	$R = \beta\text{-}C_{10}H_7$	Ia	20	Colorless needles	158—159	—	—
12	$R = \beta\text{-}C_{10}H_6O_3$	Ia	35	Yellow needles	198	4.39, 4.54	4.36
13	R = 	II	66	Colorless leaflets	212—213	4.59, 5.04	4.43
14	$R = \alpha\text{-}(4\text{-}ClC_{10}H_6)$	II	48.5	Ditto	177—177.5	4.81, 4.78	4.67
15	$R = \beta\text{-}(4\text{-}ClC_{10}H_6)$	II	46.5	" "	182—183	5.18, 5.06	4.67
16	$4\text{-}CH_3C_6H_4SO_2NHCH_2CH_2COOH$	Ia	71	Colorless needles	121.5—122	5.95, 5.86	5.76
17	$C_6H_5SO_2N(C_2H_5)CH_2COOH$	II	52.4	Ditto	162.5—163	4.79, 4.91	4.81
18	$4\text{-}CH_3C_6H_4SO_2N(CH_3)CH_2COOH$	II	75	White powder	186.5—187	5.05, 4.95	4.59
19	$CO[NHC_6H_4SO_2N(CH_3)CH_2COOH]_2$	II	60	Colorless leaflets	207—207.5	11.60, 11.30	10.89
20	$C_6H_5SO_2NHCH(C_6H_5)COOH$	II	50	White powder	120—120.5	4.74, 4.65	4.59
21	$C_6H_5SO_2N(CH_3)CH_2COOH$	II	86	Colorless needles	165.5—166	4.74, 4.60	4.59
22		II	55	Ditto	235 (with decomp)	6.74, 6.64	6.41
23		II	41	" "	209.5—211 (with decomp)	6.65, 6.71	6.41

Note: 1) Literature data: for No. 1, m.p. 165-166° [8]; for No. 5, m.p. 149° [8]; for No. 9, m.p. 148-149° [9]; for No. 11, m.p. 158-159° [10].
2) For No. 13, substitution in position 3.

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ORGANIC INSECTOFUNGICIDES

XX. THE SYNTHESIS OF MIXED ESTERS OF THIOPHOSPHORIC ACID CONTAINING HETEROCYCLIC RADICALS

K.D. Shvetsova-Shilovskaya, N.N. Melnikov and A.F. Grapov

In recent years, together with organic phosphorus compounds of the aliphatic and aromatic series, the mixed esters of thiophosphoric acid with heterocyclic hydroxy compounds are beginning to find steadily increasing use in the control of plant parasites and various harmful insects [1-3]. Of the compounds included in this type mention should first be made of the esters of thiophosphoric acid with methylhydroxycoumarin, methylchlorohydroxycoumarin and some of the heterocyclic nitrogen compounds [4-6]. Methylisopropylpyrimidinyl diethyl thiophosphate under the name of Diazinon received quite extensive use as a control agent for flies that showed resistance to DDT and other chlorinated hydrocarbons [7]. Quite recently a number of studies were published on the insecticidal properties of a large number of thiophosphoric acid esters, containing heterocyclic radicals, but information on their physicochemical properties was not shown [8,9]. The patent literature contains only abridged information on their possible preparation methods [10]. In addition, this group of compounds shows undoubted interest, since many compounds of this type are quite active insecticides and show comparatively low toxicity for warm-blooded animals [10].

In connection with the above we decided to study the synthesis of a number of mixed esters of thiophosphoric acid, containing heterocyclic radicals. We first synthesized the esters of thiophosphoric acid with the pyrazolone, pyrimidine and furan rings in the ester molecule.

The pyrimidinyl and pyrazolyl esters of thiophosphoric acid were obtained by the reaction of diethyl chlorothiophosphate with the potassium derivative of the corresponding heterocyclic compound under prolonged heating in toluene:

$$(C_2H_5O)_2PSCl + ROK \rightarrow (C_2H_5O)_2P(S)OR,$$

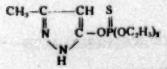
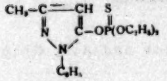
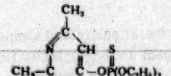
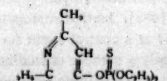
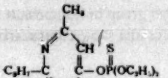
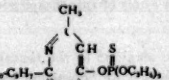
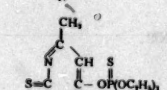
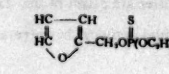
where R is the heterocyclic radical.

Furfuryl diethyl thiophosphate was synthesized by the reaction of furfuryl alcohol with diethyl chlorothiophosphate in pyridine. The compounds obtained by us and their properties are given in the table.

All of the compounds synthesized by us show quite high insecticidal activity, but several are inferior to O,O-diethyl-O-4-nitrophenyl thiophosphate (thiophos).

EXPERIMENTAL

1. Preparation of 2-alkyl-4-methylpyrimidinyl-6-diethyl thiophosphates and methylpyrazolyl diethyl thiophosphates. Preparation of mixed esters of thiophosphoric acid, containing pyrazolyl and pyrimidine rings, was carried out under the following conditions: a mixture of 0.038 mole 2-alkyl-4-methyl-6-pyrimidinone (or methylpyrazolone), 0.036 mole potash and 70 ml toluene was heated in a flask with reflux condenser and mechanical stirrer for 2 hours; the water which separated out was driven off with toluene. After driving off water, to the residue was added 7 g (0.037 mole) diethyl chlorothiophosphate and the resulting mixture was boiled for 20 hours. When the reaction was complete, the reaction mixture was treated with 20 ml water; the water was separated off and the toluene solution was washed several times with new portions of water. The wash waters were

Formula	Yield (%)	Boiling point, pressure (in mm)	n_D^{20}	d_4^{20}	Analysis for P (%)	
					found	calc.
	27	102—104 (0.08)	1.4980	1.0870	11.86 11.97	12.38
	42	125—126 (0.1)	1.5572	1.1773	9.50	9 46
	25	93—95 (0.13)	1.5010	1.1455	11.31 11.16	11.13
	28	87—92 (0.06—0.07)	1.4983	1.1350	11.31 11.52	10.64
	34	78 (0.05)	1.4941	1.1111	9.96 9.90	10.13
	29	85—90 * (0.05)	1.4922*	1.1088*	10.23 10.18	10.13
	9	132—133 (0.3)	1.5364	1.1577	9.94 9.96	10.54
	10	87—92 (0.09—0.1)	1.5001	1.0820	12.27 12.25	12.39

*From the literature: b.p. 83-84° at 0.002 mm, n_D^{20} 1.4975, d_4^{20} 1.116 [11].

extracted with benzene and the benzene extracts were combined with the main toluene solution of the substance. The solvents were driven off on a water bath in vacuum and the residue was vacuum-distilled.

2. Preparation of furfuryl diethyl thiophosphate. To a solution of 5 g furfuryl alcohol in 4 g pyridine and 5 ml benzene was added 10 g diethyl chlorothiophosphate in the course of 15 minutes with stirring and ice-water cooling. After addition of all of the cited quantity of diethyl chlorothiophosphate, the reaction mixture was held

at room temperature for 40 minutes and was heated 2 hours more on a water bath. When the reaction was complete, to the cooled mixture was added 20 ml water. The aqueous layer was extracted with benzene; the benzene was driven off in vacuum and the residue was distilled at a residual pressure of 0.1 mm. Yield about 1.5 g.

SUMMARY

A number of previously unknown mixed esters of thiophosphoric acid were synthesized, containing heterocyclic radicals. Most of the thiophosphoric acid esters synthesized by us are quite active insecticides, but several are inferior to thiophos.

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THE INTERACTION OF DIALKYLPHOSPHOROUS ACIDS WITH ALDEHYDES AND KETONES

IX. DI-TERT-(β',β',β'-TRICHLORO)-BUTYL ESTERS OF SUBSTITUTED α-HYDROXYMETHYLPHOSPHINIC ACID

V.S. Abramov and V.K. Khairullin

It was previously shown that dialkylphosphorous acids combine at the carbon-oxygen bond of the carbonyl group of aldehydes and ketones, and a scheme for this reaction was put forward [1].

We have studied the reaction of acetone chloroform with phosphorus trichloride. By this reaction we obtained the acid chloride of di-tert-(β',β',β'-trichloro)-butylphosphorous acid and the acid – well-formed white crystals with m.p. 45-46°.

In the present paper we describe the condensation of di-tert-(β',β',β'-trichloro)-butylphosphorous acid with various aldehydes and ketones, for which purpose equimolar amounts of the reactants were mixed. Since we were dealing with a solid dialkylphosphorous acid, it was necessary first of all to dissolve the acid in the other component or to conduct the reaction in a neutral solvent if the second component was a solid, as in the case of m-nitrobenzaldehyde.

The catalyst was a freshly prepared saturated solution of sodium methoxide in methyl alcohol. The reaction proceeds violently with liberation of heat. Di-tert-(β',β',β'-trichloro)-butyl esters of substituted α-hydroxymethylphosphinic acid are formed. Data for these reactions, and yields and constants of the prepared esters are set forth in Table 1.

All the esters prepared are white crystalline substances, difficultly soluble in water but soluble in common organic solvents.

When some components, such as benzaldehyde, were mixed with the acid, we observed slight heat liberation. The product started to crystallize within a few hours when the reaction mixture was stood without addition of catalyst at room temperature. Special experiments on the reaction of di-tert-(β',β',β'-trichloro)-butylphosphorous acid with some aldehydes and ketones in the absence of catalyst showed that the reaction goes slowly and is completed after a long period of time by formation of a dense crystalline mass. The progress of these reactions is detailed in Table 2.

After completion of our investigation, we became aware of an American study [2] which showed that dialkylphosphorous acids condense with chloral without a catalyst; the reaction liberates much heat and water cooling is necessary. In the cases that we studied, however, there was no external sign of reaction (liberation of heat), and the formation of the crystalline di-tert-(β',β',β'-trichloro)-butyl ester of the substituted methylphosphinic acid was only observed in course of time.

In the absence of catalyst it may be assumed that the two tautomeric forms of di-tert-(β',β',β'-trichloro)-butylphosphorous acid are present in equilibrium:

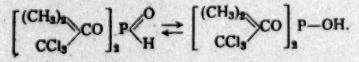
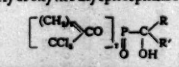


TABLE 1

Di-tert-(β',β',β'-trichloro)-butyl Esters of Substituted α-Hydroxymethylphosphinic Acid



Starting aldehyde or ketone	Radicals in the formulas of the prepared substances		Recrystallization of the prepared substances		Melting point	Yield of purified product (in %)	Chlorine content (%)		Phosphorus content (%)	
	R	R'	solvent	number of recrystallizations			found	calc.	found	calc.
Acetaldehyde	H	CH_3	Ligroine	2	118.5—120°	88.0	47.57, 47.71	47.81	6.96, 6.99	6.98
Propionaldehyde	H	C_2H_5	Ligroine	3	126—127	82.0	46.15, 46.19	46.35	6.55, 6.56	6.75
Butyraldehyde	H	C_3H_7	80% alcohol	2	133—134	62.0	44.52, 44.48	44.97	6.61, 6.52	6.55
n-Valeraldehyde	H	C_4H_9	Benzene	5	84—87	52.0	43.31, 43.27	43.68	6.08, 6.13	6.32
Isovaleraldehyde	H	iso-C_4H_9	60% alcohol	3	134—135	84.5	43.61, 43.80	43.68	6.32, 6.16	6.32
Chloral	H	CCl_3	Acetone	2	176—177	92.0	57.85, 58.05	58.25	5.54, 5.54	5.65
Benzaldehyde	H	C_6H_5	Chloroform	2	164	96.0	41.81, 41.89	41.96	6.00, 5.88	6.11
p-Tolualdehyde	H	p-$CH_3C_6H_4$	96% alcohol	2	161—162	85.0	40.79, 40.54	40.83	5.99, 5.89	5.95
Salicyclic aldehyde	H	o-HOC_6H_4	80% alcohol	2	143—144	93.0	40.46, 40.65	40.68	5.90, 6.11	5.92
m-Nitrobenzaldehyde *	H	m-$O_2NC_6H_4$	80% alcohol	2	161—162	80.0	38.86, 38.95	39.20	5.68, 5.79	5.72
Furfural	H		90% alcohol	2	143	95.0	42.75, 42.72	42.80	6.19, 6.30	6.23
Acetone	CH_3	CH_3	Acetone	2	147	98.0	46.25, 46.17	46.35	6.65, 6.67	6.75
Methyl ethyl ketone	CH_3	C_2H_5	70% alcohol	2	140	42.6	44.80, 44.99	44.97	6.58, 6.33	6.55
Acetophenone	CH_3	C_6H_5	80% alcohol	2	140—140.5	38.0	40.82, 40.65	40.83	5.71, 5.78	5.95
Cyclopentanone	$-(CH_2)_4-$		Chloroform	2	166—166.5	89.0	43.93, 43.99	43.88	6.11, 6.29	6.39
Cyclohexanone	$-(CH_2)_5-$		Chloroform	2	168.5—169	96.0	42.47, 42.59	42.62	6.01, 6.16	6.21

*Reaction conducted in ether.

In our opinion the existence of the enolic form of the acid is conditioned by the negative chlorine atoms in the tert-butyl radical which stabilize the enolic form. With progressive entry of the enolic form into reaction with carbonyl compounds, the equilibrium is shifted.

Our prepared products can evidently be utilized as insecticides since they are analogs of insecticides described in the literature [3].

TABLE 2

Preparation No.	Reacting aldehyde or ketone	Time elapsing before development of crystals from instant of mixing of reacting components (hrs)	Time in which the mixture crystallized to a dense mass (in hrs)
1	Propionaldehyde . . .	144	720
2	Chloral	6	7
3	Benzaldehyde	12	48
4	p-Tolualdehyde . . .	21	48
5	Acetone	144	932
6	Cyclopentanone . . .	208	864

SUMMARY

1. Di-tert-(β',β',β'-trichloro)-butylphosphorous acid, prepared by us, condenses with various aldehydes and ketones and forms the corresponding esters of the substituted α-hydroxymethylphosphinic acid. 16 new esters were synthesized.

2. The condensation reaction takes place both in the presence and in the absence of a catalyst.

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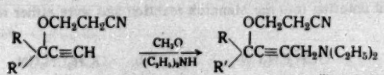
ACETYLENE DERIVATIVES

172. THE MANNICH REACTION WITH β-CYANOETHYL ETHERS OF ACETYLENIC ALCOHOLS

I.N. Nazarov and G.A. Shvekhgeimer

The Mannich reaction with acetylenic alcohols has hitherto received very little attention by investigators although the acetylenic amino alcohols obtained thereby may present interest as intermediates for the synthesis of various physiologically active substances. As was shown earlier [1], the acetylenic alcohols themselves do not readily enter into the Mannich reaction, and it is necessary first to protect the hydroxyl group [1,2]. Having at our disposal a large quantity of β-cyanoethyl ethers of various acetylenic alcohols [3], we decided it would be of interest to bring them into the Mannich reaction with the objective of preparing the corresponding acetylenic amino ethers. Reaction was effected by boiling for many hours a mixture of β-cyanoethyl ether of acetylenic alcohol with a small excess of paraform and amine in dioxane solution.

20-hour boiling of the β-cyanoethyl ether of dimethylethynyl carbinol (I, R = R' = CH_3) with a mixture of paraform and diethylamine gave a 96% yield of the β-cyanoethyl ether of 2-methyl-4-diethylaminobutyl-3-ol-2 (II, R = R' = CH_3):

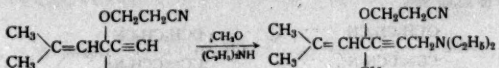


(I) (II)

R or R' = CH_3, C_2H_5, C_3H_7

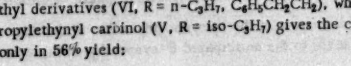
Under the same conditions the β-cyanoethyl ethers of methylethylethynyl carbinol and dipropylethynyl carbinol give the corresponding acetylenic aminoethers (II) in 91% yield.

Reaction of the β-cyanoethyl ether of methylisobutenylethenyl carbinol (III) with paraform and diethylamine gives an 81% yield of the β-cyanoethyl ether of 2,4-dimethyl-7-diethylaminohepten-2-yn-5-ol-4 (IV):



(III) (IV)

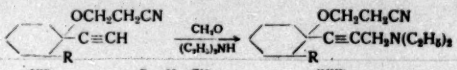
The β-cyanoethyl ethers of propylethynyl carbinol (V, R = n-C_3H_7) and β-phenylethylethenyl carbinol (V, R = $C_6H_5CH_2CH_2$) likewise react smoothly with paraform and diethylamine to form in about 80% yield the corresponding diethylaminomethyl derivatives (VI, R = n-C_3H_7, $C_6H_5CH_2CH_2$), while under the same conditions the β-cyanoethyl ether of isopropylethynyl carbinol (V, R = iso-C_3H_7) gives the corresponding β-cyanoethyl amino ether (VI, R = iso-C_3H_7) only in 56% yield:



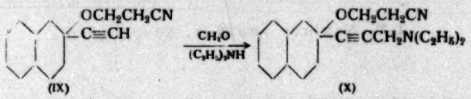
(V) (VI)

R = n-C_3H_7, iso-C_3H_7, $C_6H_5CH_2CH_2$

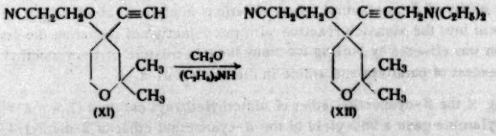
The β-cyanoethyl ether of 1-ethynylcyclohexanol (VII, R = H) reacts with paraform and diethylamine to form the acetylenic amino ether (VIII, R = H) in 96% yield:



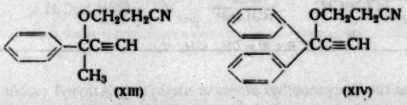
The yields of the corresponding diethylaminomethyl derivatives are lowered in presence of substituents in the cyclohexane ring. Thus, the β-cyanoethyl ether of 2-methyl-1-ethynylcyclohexanol (VII, R = CH_3) reacts with paraform and diethylamine to give the corresponding β-cyanoethyl amino ether (VIII, R = CH_3) in a yield of only 61%. The β-cyanoethyl ether of 2-ethynyldecalol-2 (IX) (which can be regarded as a derivative of a disubstituted cyclohexane) under the same conditions forms the acetylenic amino ether (X) in a yield of only 27%:



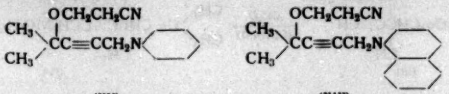
The Mannich reaction goes with great difficulty with the β-cyanoethyl ether of 2,2-dimethyl-4-ethynyltetrahydropyranol-4 (XI), and the corresponding diethylaminomethyl derivative (XII) is obtained in a yield of only 15%:



The β-cyanoethyl ethers of methylphenylethynyl carbinol and diphenylethynyl carbinol (XIII and XIV) were completely incapable of entering into the Mannich reaction and were either recovered unchanged or were resinified:

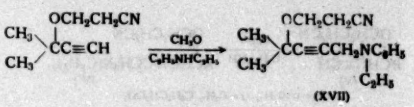


β-Cyanoethyl ethers of acetylenic alcohols similarly enter into the Mannich reaction with other aliphatic or alicyclic secondary amines. Reaction of the β-cyanoethyl ether of dimethylethynyl carbinol (I, R = R' = CH_3) with piperidine and decahydroquinoline in presence of paraform gave the corresponding acetylenic amino ethers (XV) and (XVI) in yields of about 80%.

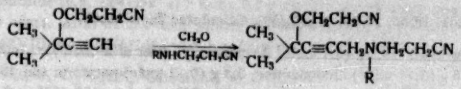


This reaction proceeds with much greater difficulty with aliphatic-aromatic secondary amines.

Thus, 25-hour boiling of a mixture of the β-cyanoethyl ether of dimethylethynyl carbinol, paraform and ethylaniline in dioxane solution leads to the anticipated β-cyanoethyl amino ether (XVII) in a yield of 50%:



The Mannich reaction proceeds with still greater difficulty in the case of secondary amines containing the β-cyanoethyl group at the nitrogen, the corresponding β-cyanoethyl amino ethers (XVIII) being obtained in yields of 30-40%.



R = CH_3, C_6H_5, o-$CH_3C_6H_4$, p-$CH_3OC_6H_4$.

(XVIII)

EXPERIMENTAL

1. A mixture of 41.1 g (0.3 mole) β-cyanoethyl ether of dimethylethynyl carbinol (b.p. 95-97° at 19 mm), 22.6 g (0.31 mole) diethylamine, 9.3 g (0.31 mole) paraform and 25 ml dioxane was boiled for 20 hours. The dioxane was driven off in the vacuum of a water-jet pump, the residue was dissolved in ether, washed with water, dried with magnesium sulfate and fractionated in vacuum. Yield 63.8 g previously described [2] β-cyanoethyl amino ether (II, R = R' = CH_3) with b.p. 118-120° at 3.5 mm.

Other experiments were carried out similarly. The reaction mixture was usually boiled for 20 hours and all changes during heating were noted in describing the experiments.

2. Taken for reaction: 15.1 g (0.10 mole) β-cyanoethyl ether of methylethylethynyl carbinol (b.p. 64-65° at 2.5 mm), 8 g (0.11 mole) diethylamine, 3.3 g (0.11 mole) paraform and 10 ml dioxane. Yield 21.5 g β-cyanoethyl amino ether (II, R = CH_3, R' = C_2H_5) with b.p. 134-135° at 3.5 mm, n_D^{20} 1.4600, d_4^{20} 0.9201, MR_D 70.25; calc. 70.19.

Found %: N 11.85, 11.66. $C_{14}H_{24}ON_2$. Calculated %: N 11.86.

3. Taken for reaction: 14.3 g (0.074 mole) β-cyanoethyl ether of dipropylethynyl carbinol (b.p. 102-103° at 5 mm), 8 g (0.11 mole), diethylamine, 3.3 g (0.11 mole) paraform and 10 ml dioxane. Yield 18.8 g β-cyanoethyl amino ether (II, R = R' = n-C_3H_7) with b.p. 152-153° at 3.5 mm, n_D^{20} 1.4615, d_4^{20} 0.9079, MR_D 84.10; calc. 84.04.

Found %: N 10.06, 10.08. $C_{17}H_{30}ON_2$. Calculated %: N 10.07.

4. Taken for reaction: 17 g (0.096 mole) β-cyanoethyl ether of methylisobutenylethynyl carbinol (III) (b.p. 98-100° at 5 mm), 8 g (0.11 mole) diethylamine, 3.3 g paraform (0.11 mole) and 10 ml dioxane. Yield 20.3 g β-cyanoethyl amino ether (IV) with b.p. 135-137° at 2 mm, n_D^{20} 1.4735, d_4^{20} 0.9304, MR_D 79.04; calc. 78.96.

Found %: N 10.59, 10.87, 10.89. $C_{16}H_{26}ON_2$. Calculated %: N 10.68.

5. Taken for reaction: 15.1 g (0.1 mole) β-cyanoethyl ether of propylethynyl carbinol (b.p. 90-91° at 6 mm), 8 g (0.11 mole) diethylamine, 3.3 g (0.11 mole) paraform and 10 ml dioxane. Yield 19.4 g β-cyanoethyl amino ether (VI, R = n-C_3H_7) with b.p. 134-136° at 2.5 mm, 150-151° at 5 mm, n_D^{20} 1.4612, d_4^{20} 0.9198, MR_D 70.46; calc. 70.19.

Found %: N 11.73, 11.75. $C_{14}H_{24}ON_2$. Calculated %: N 11.86.

6. Taken for reaction: 20.2 g (0.1 mole) β-cyanoethyl ether of β-phenylethylethynyl carbinol (b.p. 141-143° at 3 mm), 8 g (0.11 mole) diethylamine, 3.3 g (0.11 mole) paraform and 10 ml dioxane. Yield 23.1 g β-cyanoethyl amino ether (VI, R = $C_6H_5CH_2CH_2$) with b.p. 192-194° at 2 mm, n_D^{20} 1.5100, d_4^{20} 0.9915, MR_D 89.89; calc. 89.68.

Found %: N 9.28, 9.34. $C_{20}H_{26}ON_2$. Calculated %: N 9.39.

7. Taken for reaction: 7.5 g (0.05 mole) β-cyanoethyl ether of isopropylethynyl carbinol (b.p. 83-85° at 6 mm), 4 g (0.05 mole) diethylamine, 1.65 g (0.05 mole) paraform and 5 ml dioxane. Yield 6.7 g β-cyanoethyl aminoether (VI, R = iso-C_3H_7) with b.p. 148-150° at 8 mm, 136-138° at 4 mm, n_D^{20} 1.4608, d_4^{20} 0.9198, MR_D 70.38; calc. 70.19.

Found %: N 11.88, 11.67. $C_{14}H_{24}ON_2$. Calculated %: N 11.86.

8. Taken for reaction: 17.7 g (0.1 mole) β-cyanoethyl ether of 1-ethynylcyclohexanol (b.p. 92-95° at 3 mm), 8 g (0.11 mole) diethylamine, 3.3 g (0.11 mole) paraform and 10 ml dioxane. Yield 25.1 g β-cyanoethyl amino ether (VIII, R = H) with b.p. 148-150° at 2 mm, 168-170° at 6 mm; n_D^{20} 1.4817, d_4^{20} 0.9652, MR_D 77.34; calc. 77.23.

Found %: N 10.51, 10.50, 10.60. $C_{15}H_{26}ON_2$. Calculated %: N 10.69.

9. Taken for reaction: 19.1 g (0.1 mole) β-cyanoethyl ether of 2-methyl-1-ethynylcyclohexanol (b.p. 133-136° at 15 mm), 8 g (0.11 mole) diethylamine, 3.3 g (0.11 mole) paraform and 15 ml dioxane. Yield 16.9 g β-cyanoethyl amino ether (VIII, R = CH_3) with b.p. 172-175° at 5 mm, 156-157° at 2.5 mm; n_D^{20} 1.4791, d_4^{20} 0.9582, MR_D 81.69; calc. 81.84.

Found %: N 9.89, 10.04. $C_{17}H_{28}ON_2$. Calculated %: N 10.15.

8.1 g initial β-cyanoethyl ether returned unchanged from the experiment.

10. Taken for reaction: 19 g (0.08 mole) β-cyanoethyl ether of 2-ethynyldecalol-2 (IX) (b.p. 150-153° at 4.5 mm), 7.3 g (0.1 mole) diethylamine, 3 g (0.1 mole) paraform and 10 ml dioxane. Yield 7.4 g β-cyanoethyl amino ether (X) with b.p. 194-197° at 5 mm, n_D^{20} 1.5012, d_4^{20} 1.0013, MR_D 93.01; calc. 93.49.

Found %: N 8.45, 8.57. $C_{20}H_{32}ON_2$. Calculated %: N 8.86.

10.6 g initial β-cyanoethyl ether returned unchanged from the experiment.

11. Taken for reaction: 20.7 g (0.1 mole) β-cyanoethyl ether of 2,2-dimethyl-4-ethynyltetrahydropyranol-4 (XI)(b.p. 122-125° at 3 mm), 8 g (0.11 mole) diethylamine, 3.3 g (0.11 mole) paraform and 10 ml dioxane. Yield 4.5 g β-cyanoethyl amino ether (XII) with b.p. 170-173° at 3 mm, n_D^{20} 1.4831, d_4^{20} 1.0197, MR_D 81.79; calc. 81.84.

Found %: N 9.70. $C_{17}H_{28}O_2N_2$. Calculated %: N 9.59.

12.1 g initial β-cyanoethyl ether returned unchanged from the experiment.

12. A mixture of 13.7 g (0.1 mole) β-cyanoethyl ether of dimethylethynyl carbinol, 9 g (0.107 mole) β-cyanoethylmethylamine, 3.3 g (0.11 mole) paraform and 10 ml dioxane was boiled for 25 hours. Yield 5.7 g β-cyanoethyl amino ether (XVIII, R = CH_3) with b.p. 182-184° at 5 mm, n_D^{20} 1.4715, d_4^{20} 0.9967, MR_D 65.40; calc. 65.39.

Found %: N 18.76, 18.53. $C_{10}H_{18}ON_2$. Calculated %: N 18.10.

10.2 g initial β-cyanoethyl ether returned unchanged from the experiment.

13. Taken for reaction: 13.7 g (0.1 mole) β-cyanoethyl ether of dimethylethynyl carbinol, 9.5 g (0.11 mole) piperidine, 3.3 g (0.11 mole) paraform and 10 ml dioxane. Yield 19 g β-cyanoethyl amino ether (XV) with b.p. 148-150° at 4 mm, n_D^{20} 1.4807, d_4^{20} 0.9742, MR_D 68.32; calc. 67.99.

Found %: N 10.86, 10.83. $C_{14}H_{22}ON_2$. Calculated %: N 10.96.

14. Taken for reaction: 13.7 g (0.1 mole) β-cyanoethyl ether of dimethylethynyl carbinol, 15.3 g (0.11 mole) decahydroquinoline, 3.3 g (0.11 mole) paraform and 10 ml dioxane. Yield 23.9 g β-cyanoethyl amino ether (XVI) with b.p. 183-185° at 5 mm, n_D^{20} 1.4953, d_4^{20} 0.9968, MR_D 84.30; calc. 84.26.

Found %: N 9.35, 9.75. $C_{19}H_{30}ON_2$. Calculated %: N 9.72.

15. A mixture of 13.7 g (0.1 mole) β-cyanoethyl ether of dimethylethynyl carbinol, 13 g (0.11 mole) ethylaniline, 3.3 g (0.11 mole) paraform and 10 ml dioxane was boiled for 15 hours. After each 5-hour period, to the reaction mixture was added 0.2 g paraform. Yield 13.3 g amino ether (XVII) with b.p. 168-170° at 2 mm, n_D^{20} 1.5312, d_4^{20} 1.0148.

Found %: N 10.12, 10.24. $C_{17}H_{22}ON_2$. Calculated %: N 10.38.

16. A mixture of 13.7 g (0.1 mole) β-cyanoethyl ether of dimethylethynyl carbinol, 16.1 g (0.11 mole) β-cyanoethylaniline (b.p. 128-130° at 2.5 ml), 3.3 g (0.11 mole) paraform and 10 ml dioxane was boiled for 25 hours. After each 5-hour period, to the reaction mixture was added 0.2 g paraform. Yield 11.2 g aminoether (XVIII, R = C_6H_5) with b.p. 228-232° at 4 mm, n_D^{20} 1.5445, d_4^{20} 1.0746.

Found %: N 13.88, 13.83. $C_{19}H_{21}ON_3$. Calculated %: N 14.24.

6.7 g initial β-cyanoethyl ether and 3.3 g β-cyanoethylaniline were returned from the experiment.

17. Taken for reaction: 13.7 g (0.1 mole) β-cyanoethyl ether of dimethylethynyl carbinol, 17.6 g (0.11 mole) β-cyanoethyl-o-toluidine (b.p. 128-130° at 3 mm), 3.3 g (0.11 mole) paraform and 10 ml dioxane. The mixture was boiled for 25 hours. After each 5-hour period, to the reaction mixture was added 0.2 g paraform. Yield 12.2 g amino ether (XVIII, R = o-$CH_3C_6H_4$) with b.p. 230-234° at 3 mm, n_D^{20} 1.5213, d_4^{20} 1.0438.

Found %: N 13.55, 13.43. $C_{20}H_{22}ON_2$. Calculated %: N 13.59.

6.3 g initial β-cyanoethyl ether and 7.2 g β-cyanoethyl-o-toluidine returned from the experiment.

18. Taken for reaction: 13.7 g (0.1 mole) β-cyanoethyl ether of dimethylethynyl carbinol, 19.8 g (0.11 mole) β-cyanoethyl-p-anisidine (b.p. 158-160° at 3 mm), 3.3 g (0.11 mole) paraform and 10 ml dioxane. The mixture was boiled for 25 hours. After each 5-hour period, to the reaction mixture was added 0.2 g paraform. Yield 10.4 g amino ether (XVIII, R = p-$CH_3OC_6H_4$) with b.p. 258-263° at 5 mm, n_D^{20} 1.5600, d_4^{20} 1.1132.

Found %: N 12.38, 12.62. $C_{20}H_{22}O_2N_2$. Calculated %: N 12.92.

8.8 g initial β-cyanoethyl ether and 8.2 g β-cyanoethyl-p-anisidine returned from the experiment.

SUMMARY

The Mannich reaction with β-cyanoethyl ethers of various acetylenic alcohols is described, and it is shown that the yield of the resultant dialkylaminomethyl derivatives depends both upon the character of the acetylenic alcohol and upon that of the secondary amine. This reaction proceeds the most smoothly with aliphatic derivatives (yield 80-96%). β-Cyanoethyl ethers of methylphenylethynyl carbinol and diphenylethynyl carbinol are completely incapable of entering into the Mannich reaction. Secondary amines containing aromatic and β-cyanoethyl radicals undergo the reaction with much less facility than aliphatic amines.

LITERATURE CITED

[1] E.R.H. Jones, J. Marszak and H. Bader, J. Chem. Soc., 1578 (1947).

[2] E.S. Lagucheva, and K.D. Petrov, J. Gen. Chem., Supp. II, 1347 (1953).

[3] I.N. Nazarov and G.A. Shvekhgeimer, J. Gen. Chem., 25, 504 (1955)(T.p. 471).*

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Academy of Sciences of USSR

*T.p. = C.B. Translation pagination.

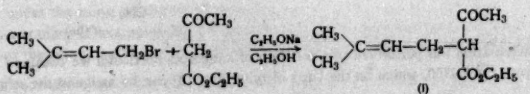
THE SYNTHESIS OF STEROIDS AND RELATED COMPOUNDS

XXXI. CONDENSATION OF HALOGEN DERIVATIVES OF THE ALLYL TYPE WITH CYCLIC 1,3-DIKETONES AND INNER-MOLECULAR CYCLIZATION (WITH LOSS OF WATER) OF THE RESULTANT COMPOUNDS

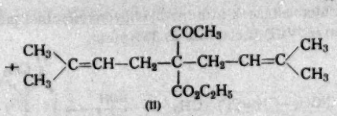
I.N. Nazarov, S.N. Ananchenko and I.V. Torgov

The present work is a continuation of investigations on the synthesis of polycyclic compounds related to the steroids. It appeared of interest to investigate the condensation of cyclic 1,3-diketones with halo-derivatives of the allyl type and to establish the possibility of cyclization of the resultant products. As we know, cyclohexane-1,3-dione (dihydroresorcinol) usually exists in solution in the enol form. Thus, in aqueous solution 95.3% is in the enol form [1]; we should therefore expect that in the first instance the alkylation of dihydroresorcinol would proceed in the direction of formation of the enol ether, as was also confirmed by the studies of Merling [2]. Formation of C-substituted derivatives of dihydroresorcinol was known up to recently only in two cases: reaction of the sodium derivative of dihydroresorcinol with benzaldehyde [3] and with allyl bromide [4]. And only very recently, after we had started our research, were some investigations on the synthesis of mono- and dialkyl-substituted dihydroresorcinols reported by Stetter and Dierichs [4]. As the allylic halogen derivatives for this condensation we selected 2-methyl-4-chloro-butene-2; 2-methyl-4-bromobutene-2; 1,3-dichlorobutene-2, and crotyl bromide.

The relative susceptibility to condensation of these halo-derivatives was initially investigated with reference to the ethyl esters of acetoacetic and methylacetoacetic acids. Condensation of 2-methyl-4-bromobutene-2 with sodium acetoacetic ester gives a 66% yield of γ,γ-dimethylallyl acetoacetic esfer (I); in addition about 5% of a disubstituted acetoacetic ester (II) could be isolated:



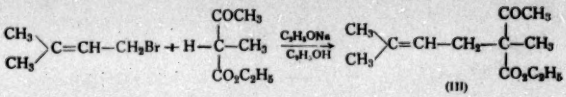
(I)



(II)

In the analogous condensation of acetoacetic ester with 2-methyl-4-chlorobutene-2 the yield of γ,γ-dimethylallyl acetoacetic ester (I) fell to 40%.

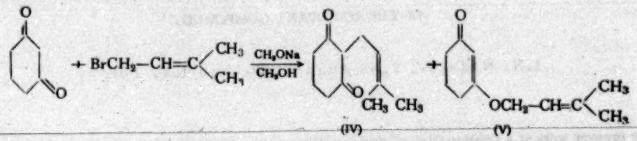
Condensation of methylacetoacetic ester with 2-methyl-4-bromobutene-2 gives the corresponding disubstituted acetoacetic ester (III) in 75% yield:



(III)

Replacement of 2-methyl-4-bromobutene-2 by 2-methyl-4-chlorobutene-2 in this condensation likewise lowers the yield of ester (III) to 45%.

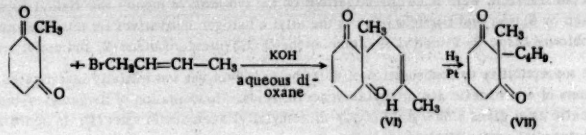
Condensation of dihydroresorcinol with 2-methyl-4-bromobutene-2 in presence of sodium methoxide in methanol gave two products – a C-substituted derivative of dihydroresorcinol (IV) and an O-substituted derivative (V) in yields of 40 and 17%, respectively. The structure of the enol ether (V) was confirmed by its hydrolysis to the original dihydroresorcinol with dilute hydrochloric acid:



(IV) (V)

It is interesting that in the condensation of dihydroresorcinol with 2-methyl-4-chlorobutene-2 the yield of C-substituted derivative (IV) falls to 12% while the yield of enol ether (V) rises to 31%.

Condensation of 1-bromobutene-2 (crotyl bromide) with methyldihydroresorcinol can only be effected with the help of potassium hydroxide in aqueous dioxane solution. A 27% yield is then obtained of 2-methyl-2-crotylcyclohexane-1,3-dione (VI), which on hydrogenation in alcohol in presence of platinum catalyst absorbs 1 mole hydrogen and is converted into 2-methyl-2-butylcyclohexane-1,3-dione (VII):

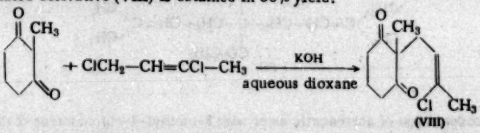


(VI) (VII)

$CH_3CH{=}CHCH_2CHCO(CH_2)_3CO_2CH_3$ (VIIa)

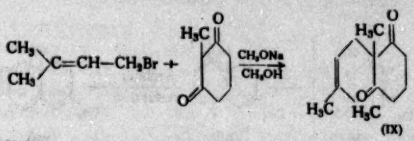
When this condensation was performed in a medium of anhydrous methanol we obtained a liquid with b.p. 109.5-111° at 3.5 mm, n_D^{20} 1.4750, which on the basis of other data [5] can be assigned the structure of (VIIa).

The condensation of 1,3-dichlorobutene-2 with methyldihydroresorcinol proceeds in an entirely similar manner. The disubstituted derivative (VIII) is obtained in 35% yield:



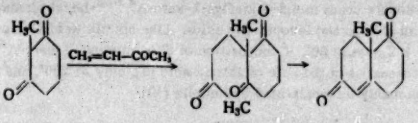
(VIII)

Condensation of the sodium derivative of methyldihydroresorcinol with 2-methyl-4-bromobutene-2 leads to a 67% yield of 2-methyl-2-(γ,γ-dimethylallyl)-cyclohexane-1,3-dione (IX). When this condensation is performed with 2-methyl-4-chlorobutene-2, likewise in aqueous dioxane solution [in a manner similar to the preparation of diketones (VI) and (VIII)], the yield of Compound (IX) falls to 33-36%.



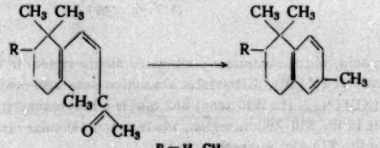
(IX)

After studying the condensation of allylic halo-derivatives with dihydroresorcinol and methyldihydroresorcinol, we turned our attention to the reaction of cyclization of the prepared products. As we know, the presence of an adjacent carbonyl group makes the α-atoms of hydrogen more labile, so that they become capable of entering into various reactions such as the crotonic condensation. On this basis we developed in our laboratory a method of synthesis of 9-methyl-1,6-diketo-Δ^5-octalin [6]:



It was of interest to establish whether cyclic 1,3-diketones containing in the side chain a double bond in place of the carbonyl group are capable of a similar intramolecular condensation.

Only three cases of such a type of cyclization have been reported in the literature – the cyclization of β-ionone, irone [7] and methylheptenone [8] respectively to ionene, irene (in presence of hydriodic acid and phosphorus) and dihydro-m-xylene under the action of 75% sulfuric acid:

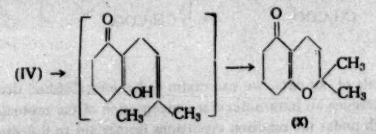


R = H, CH_3

We realized the cyclization of γ,γ-dimethylallyl acetoacetic ester (I) with the help of 75% sulfuric acid and so obtained dihydro-m-xylene in 19% yield; the constants of the product agreed with those of Verley's preparation [8], obtained by cyclization of methylheptenone. The structure of dihydro-m-xylene was confirmed by its transformation into 1,3-dimethyl-2-nitrobenzene.

Cyclization under the same conditions of disubstituted cyclohexanediones, however, was found impossible, since, as shown in a number of examples [6], the cyclohexanedione ring is ruptured under the action of both acids and alkalies. It was therefore decided to investigate phosphorus pentoxide as a dehydrating agent.

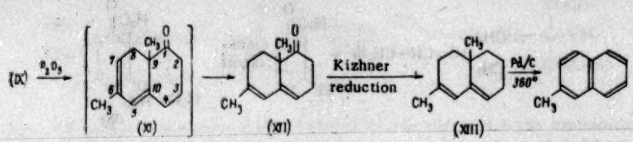
Heating of 2-(γ,γ-dimethylallyl)-cylcohexane-1,3-dione (IV) in vacuum in presence of phosphorus pentoxide (0.6% of the weight of substance taken) led to formation in 77% yield of 2,2-dimethyltetrahydrochroman-5-one (X):



(X)

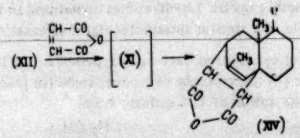
We did not succeed in cyclizing 2-methyl-2-crotylcyclohexane-1,3-dione (VI) and 2-methyl-2-(γ-crotyl)-cyclohexane-1,3-dione (VIII) by heating (120-160°) with phosphorus pentoxide, probably due to the trans-arrangement of the methyl group in the crotyl radical in relation to the carbonyl of the cyclohexane ring [as indicated in formulas (VI) and (VIII)].

Heating of 2-methyl-2-(γ,γ-dimethylallyl)-cyclohexane-1,3-dione (IX) in vacuum in presence of phosphorus pentoxide (0.5% of weight of substance) led to a 30% yield of 6,9-dimethyl-1-keto-$\Delta^{(10),5}$-hexahydronaphthalene (XII) with m.p. 50°:



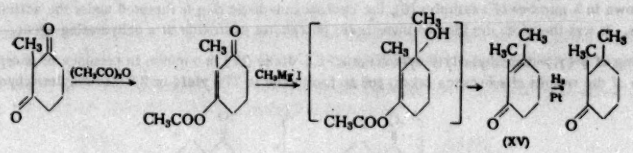
The structure of 6,9-dimethyl-1-keto-$\Delta^{4(10),5}$-hexahydronaphthalene (XII) was demonstrated by Kizhner reduction to 6,9-dimethyl-$\Delta^{4(10),5}$-hexahydronaphthalene (XIII), which was then dehydrogenated with palladium on carbon at 360-370° to the known 2-methylnaphthalene.

The position of the double bonds in 6,9-dimethyl-1-keto-$\Delta^{4(10),5}$-hexahydronaphthalene (XII) is assumed on the basis of analogy with abietic and levopimaric acids. Like abietic acid, Compound (XII) is unstable and oxidizes after keeping for 1-2 days at 20°. Condensation of 6,9-dimethyl-1-keto-$\Delta^{4(10),5}$-hexahydronaphthalene with maleic anhydride proceeds, as in the case of abietic acid [9], only at 200°, and leads to a 35% yield of the adduct (XIV), which can probably be represented by Formula (XI):



As we know, levopimaric acid, which contains a conjugated dienic system in one ring [like Compound (XI)], reacts with maleic anhydride even at 20° [10]. Ultraviolet absorption data also confirm that 6,9-dimethyl-1-keto-$\Delta^{4(10),5}$-hexahydronaphthalene (XII) [λ_{max} (in isooctane) 252 mμ] is a heteroannular transoid diene. For the latter the absorption maximum lies in the 230-250mμ region, whereas homoannular cisoid dienes of the type of (XI) have an absorption maximum in the 270-280 mμ region [11].

The unusual character of 6,9-dimethyl-1-keto-$\Delta^{4(10),5}$-hexahydronaphthalene (XII) is also manifested in its inability, under normal conditions, to condense even with acetylides of alkali metals in liquid ammonia, whereas nearly all aldehydes and ketones, including the enol ethers of methyldihydroresorcinol [12], undergo this reaction. The enol ethers of methyldihydroresorcinol also enter into reaction with Grignard reagents, as we showed in the following example:



Consequently, on the basis of our data, we can claim to have established that diketone (IX) when heated with phosphorus pentoxide undergoes an intramolecular condensation of the crotonic type with formation of an intermediate ketone (XI) which under the reaction conditions isomerizes to 6,9-dimethyl-keto-$\Delta^{4(10),5}$-hexahydronaphthalene (XII), similarly to the isomerization of levopimaric acid to abietic acid under the influence of acids and heat.

The new condensation reaction that we have discovered may be utilized for the synthesis of steroids and related compounds.

EXPERIMENTAL

Preparation of 2-methyl-4-bromobutene-2. Into 50 g dimethylvinyl carbinol (b.p. 97-98°) was passed at at 0° a stream of hydrogen bromide until the weight addition of the reaction mass reached 50 g (47 g in theory). The bromide was separated from the water that formed, the aqueous layer was extracted with ether, the combined ethereal extracts were neutralized with soda (bicarbonate) and dried with potash. After distillation, 66 g 2-methyl-4-bromobutene-2 was obtained with b.p. 61-63° at 67 mm, n_D^{20} 1.4900 [13]. Yield 74%.

Preparation of 2-methyl-4-chlorobutene-2. 2-Methyl-4-chlorobutene-2 was prepared by the same method that was described previously [14]. From 100 g dimethylvinyl carbinol was obtained 74 g 2-methylchlorobutene-2 with b.p. 62-64° at 150 mm, n_D^{20} 1.4498 (the product was fractionated on a column of the Fenske type with glass packing). Yield 56%.

Condensation of sodium acetoacetic ester with 2-methyl-4-bromobutene-2. In a 3-necked flask, fitted with mechanical stirrer, dropping funnel, thermometer and reflux condenser was prepared a solution of sodium alcoholate from 4.6 g sodium and 56 ml anhydrous alcohol. To the cooled solution of sodium alcoholate was added 26 g acetoacetic ester and the reaction mixture was stirred at 20° for 1 hour. Then in the course of 15 minutes was added 38 g 2-methyl-4-bromobutene-2 and the solution warmed up to 60-65°. The reaction mass was stirred for 1 hour at room temperature and for 1 hour was heated on a boiling water bath. The alcohol was driven off under a slight vacuum and to the residue was added 50 ml water; the supernatant layer of oil was separated and the aqueous layer was extracted 3 times with ether and the combined ethereal extract was washed with water and dried with magnesium sulfate. After driving off the ether the product was vacuum-fractionated: 1st fraction had b.p. 43-54° at 8 mm, n_D^{18} 1.4315 (1.5 g); 2nd fraction b.p. 54-111° at 8 mm, n_D^{18} 1.4382 (3 g); 3rd fraction b.p. 112-114° at 8 mm, n_D^{18} 1.4529 (27 g); 4th fraction b.p. 114-143° at 8 mm, n_D^{18} 1.4700 (5 g); residue 2 g.

The third fraction was pure ethyl ester of γ,γ-dimethylallylacetoacetic acid (I), b.p. 112-114° at 8 mm, 86° at 1 mm, n_D^{18} 1.4529, d_4^{20} 0.9751, MR_D 55.08; calc. 54.84. Yield 66%.

Found %: C 66.72, 66.40; H 9.17, 9.15. $C_{11}H_{18}O_3$. Calculated %: C 66.62; H 9.15.

The fourth fraction was again distilled in vacuum and 3 g ethyl ester of di-(γ,γ-dimethylallyl)-acetoacetic acid (II) was obtained with b.p. 128-130° at 1 mm, n_D^{20} 1.4700, d_4^{20} 0.9544, MR_D 77.01; calc. 76.81. Yield 5%.

Found %: C 72.37, 72.35; H 9.93, 10.10. $C_{16}H_{26}O_3$. Calculated %: C 72.18; H 9.83.

Condensation of sodium acetoacetic ester with 2-methyl-4-chlorobutene-2. The condensation was carried out in the same manner as in the preceding experiment, starting from 18 g acetoacetic ester and 18 g chloride except that the reaction mixture was boiled for 2.5 hours. Fractionation yielded the following fractions: 1st fraction with b.p. 52-113° at 11 mm, n_D^{20} 1.4288 (2 g); second fraction with b.p. 113-117° at 11 mm, n_D^{20} 1.4468 (1 g); 3rd fraction with b.p. 118-120° at 11 mm, n_D^{20} 1.4520 (11 g); 4th fraction with b.p. 120-140° at 11 mm, n_D^{20} 1.4610 (6 g); residue 3.5 g.

The third fraction was the above-described ethyl ester of dimethylallylacetoacetic acid (I). Yield 41%.

Cyclization of ethyl ester of γ,γ-dimethylallylacetoacetic acid (I) [8]. 15 g ethyl ester of γ,γ-dimethylallylacetoacetic acid and 22.5 g 75% sulfuric acid was stirred for 15 minutes; the liquid warmed up to 60° and carbon dioxide evolved. The reaction mass was poured into 50 ml water and extracted with ether. The ethereal extract was washed three times with saturated soda solution, then with water and was dried with calcium chloride. Fractionation yielded the following fractions: 1st fraction with b.p. 63° at 60 mm, n_D^{18} 1.4415 (2 g); 2nd fraction b.p. 63-66° at 10 mm, n_D^{18} 1.4495 (1.5 g); 3rd fraction with b.p. 82-130° at 1.5 mm, n_D^{18} 1.4870 (1 g); 4th fraction with b.p. 130-170° at 1.5 mm, n_D^{18} 1.4980 (1 g).

On further heating the residue decomposed.

The first two fractions were distilled over metallic sodium and we obtained 1.5 g dihydro-m-xylene with b.p. 129-130° at 760 mm, n_D^{20} 1.4430, d_4^{20} 0.8283. Yield 19%.

Literature data [15] on dihydro-m-xylene give b.p. 131° at 760 mm, n_D^{25} 1.4410, d_4^{20} 0.838.

Nitration of dihydro-m-xylene. 0.9 g dihydro-m-xylene was poured into a nitrating mixture, prepared from 6.5 g 56% nitric acid and 19.4 g concentrated sulfuric acid. The hydrocarbon instantly dissolved and a violent evolution of nitrogen oxides was observed. The mixture was heated for 5 minutes at 50° and poured into cold

water. 0.41 g of oil was obtained which crystallized upon standing. After 2 fractional distillations from alcohol, 0.2 g 1,3-dimethyl-2-nitrobenzene was obtained with m.p. 74-75°. A melting test mixture with a known sample melted at 74-75°.

Condensation of sodium methylacetoacetic ester with 2-methyl-4-bromobutene-2. In a 3-necked flask fitted with mechanical stirrer, dropping funnel, thermometer and reflux condenser was prepared a solution of sodium alcoholate from 4.6 g sodium and 56 ml anhydrous alcohol. To the cooled solution of sodium alcoholate was added 28.8 g methylacetoacetic ester (b.p. 74-75° at 11 mm, n_D^{19} 1.4213 [16]). A viscous white precipitate of sodium derivative instantly formed with evolution of heat. The reaction mass was heated on a water bath for 1 hour, cooled, and in the course of 15 minutes 33 g 2-methyl-4-bromobutene-2 was added; the reaction mass heated up to 60-65°. The reaction mass was stirred for 1 hour at room temperature and 2 hours with heating on a boiling water bath. The alcohol was driven off under a slight vacuum and to the residue was added 50 ml water and the product was extracted 3 times with ether. The combined ethereal extracts were washed 2 times with saturated soda solution, then with water and dried with magnesium sulfate. Ether was driven off and the residue was vacuum-distilled. The 1st fraction had b.p. 34-67° at 8 mm, n_D^{20} 1.4240 (3.5 g); the 2nd fraction had b.p. 67-111° at 8 mm, n_D^{22} 1.4290 (3.1 g); 3rd fraction, b.p. 112-114° at 8 mm, n_D^{22} 1.4508 (31 g); residue 2 g.

The 3rd fraction was the ethyl ester of methyl-γ,γ-dimethylallylacetoacetic acid (III), b.p. 112-114° at 8 mm, 94.5° at 15 mm, n_D^{20} 1.4515, d_4^{20} 0.9616, MR_D 58.69; calc. 59.41. Yield 75%.

Found %: C 67.70, 67.89; H 9.45, 9.52. $C_{12}H_{20}O_3$. Calculated %: C 67.89; H 9.49.

Condensation of sodium methylacetoacetic ester with 2-methyl-4-chlorobutene-2. The condensation was carried out in the same manner as in the preceding experiment starting from 20 g methylacetoacetic ester and 18 g 2-methyl-4-chlorobutene-2 except that the reaction mixture was boiled for 2.5 hours. Fractionation yielded the following fractions: 1st fraction b.p. 56-80° at 1 mm, n_D^{21} 1.4420 (5 g); 2nd fraction b.p. 80-92° at 1 mm, n_D^{21} 1.4490 (1 g); 3rd fraction b.p. 92-93° at 1 mm, n_D^{21} 1.4508 (13 g); residue 3 g.

The 3rd fraction was the ethyl ester of methyl-γ,γ-dimethylallylacetoacetic acid (III). Yield 45%.

Attempts were made to effect the cyclization of this ester by the action of: 1) phosphoric acid (d 1.83) and phosphoric anhydride at 80° for 30 minutes, 2) piperidine butyrate at 135° in vacuum (50 mm) for 3 hours, 3) finely ground potassium bisulfate at 160-170° in vacuum (100 mm) for 4 hours; 4) acetic anhydride (in a metal ampul at 170-175°) for 10 hours; 5) phosphoric anhydride (0.5% by weight of taken ester) on boiling water bath in vacuum (20 mm) for 3 hours. In all cases either resinification products or returned initial ester (in Experiments 2,3 and 4) were obtained.

Condensation of dihydroresorcinol with 2-methyl-4-bromobutene-2. Dihydroresorcinol was prepared by the previously described method [17]. In a 3-necked flask fitted with mechanical stirrer, dropping funnel and reflux condenser was prepared a solution of sodium alcoholate from 3.1 g sodium in 34 ml anhydrous methanol. To the cooled solution of sodium methylate was added 15 g dihydroresorcinol (m.p. 102-103°); the mixture was heated on a water bath for 15 minutes. The solution was cooled and to it added in the course of 15 minutes 22 g 2-methyl-4-bromobutene-2; the reaction mass heated up to 65-70° and in the course of 5 minutes its color sharply changed from yellow through bright-red to colorless. The reaction mass was stirred at room temperature for 1 hour. The alcohol was driven off under a slight vacuum and to the residue was added 200 ml 3% solution of caustic soda and the product was carefully extracted with ether. The ethereal extract was washed with water and dried with magnesium sulfate. The aqueous solution was acidified at 0° with concentrated hydrochloric acid until the reaction was slightly acid on Congo. The crystals which came down were separated off and washed with several portions of cold water. Yield 9.5 g 2-(γ,γ-dimethylallyl)-cyclohexane-1,3-dione (IV) with m.p. 137-139°. Yield 40%. The pure diketone had m.p. 140° (from 50% methanol).

Found %: C 73.34, 73.15; H 8.71, 8.84. $C_{11}H_{16}O_2$. Calculated %: C 73.29; H 8.94.

The substance gave a violet coloration with an alcoholic solution of ferric chloride and was unchanged by the action of hydrochloric acid in the cold. Fractionation of the ethereal extract of neutral products yielded: 1st fraction b.p. 64-94° at 1 mm, n_D^{20} 1.4990 (0.5 g); 2nd fraction b.p. 94-95° at 1 mm, n_D^{20} 1.5010 (4.2 g); residue 1 g.

The 2nd fraction was 1-(γ,γ-dimethylallyloxy)-Δ'-cyclohexen-3-one (V), b.p. 94-95° at 1 mm, n_D^{20} 1.5010, d_4^{20} 1.0212, MR_D 51.51; calc. 51.97. Yield 17%.

Found %: C 73.45, 73.25; H 9.14, 9.03. $C_{11}H_{16}O_2$. Calculated %: C 73.29; H 8.94.

The action of 3% hydrochloric acid on enol ether (V) brought about its hydrolysis with formation of cyclohexan-1,3-dione (m.p. 100-101°).

Condensation of dihydroresorcinol with 2-methyl-4-chlorobutene-2. Condensation and separation of the products were carried out in the same manner as for preparation of (IV) and (V). 5 g dihydroresorcinol was taken for reaction with 6 g 2-methyl-4-chlorobutane-2, but the reaction mixture was boiled for 1 hour. We obtained 1 g 2-(γ,γ-dimethylallyl)-cyclohexane-1,3-dione (IV) with m.p. 139-140° (yield 12%) and 2.5 g 1-(γ,γ-dimethylallyloxy)-Δ'-cyclohexen-3-one (V) with b.p. 120-122° at 4 mm, n_D^{20} 1.5010 (yield 31%).

Cyclization of 2-(γ,γ-dimethylallyl)-cyclohexane-1,3-dione (IV). A mixture of 9 g 2-(γ,γ-dimethylallyl)-cyclohexane-1,3-dione (IV) (m.p. 139-140°) and 0.6 g phosphoric anhydride was heated in vacuum (10 mm) for 1.5 hours at 116-120°. The refractive index in this time changed from 1.4910 to 1.5260 and did not rise further. The reaction mass was treated with a saturated solution of soda, extracted with ether, the ethereal extracts were washed with water and dried with magnesium sulfate. The ether was driven off and the residue was distilled in vacuum; we obtained 7 g 2,2-dimethyltetrahydrochroman-5-one (X) with b.p. 93-94° at 2 mm; n_D^{20} 1.5220, d_4^{20} 1.0930, MR 50.23; calc. 49.78. Yield 77%

Found %: C 73.29, 73.37; H 9.13, 8.90. $C_{11}H_{16}O_2$. Calculated %: C 73.29; H 8.94.

The semicarbazone was in the form of lustrous white crystals which had m.p. 219° with decomposition (from mixture of alcohol and dioxane).

Found %: N 17.98, 17.95. $C_{12}H_{19}O_2N_3$. Calculated %: N 17.70.

2,4-Dinitrophenylhydrazone had m.p. 240-241°, $\lambda_{max.}$ (in isooctane) 373 mμ ($\varepsilon_{max.}$ 23000).

Condensation of methyldihydroresorcinol with 1-bromobutene-2. Methyldihydroresorcinol was prepared by dihydroresorcinol methylation according to the method described by I.N. Nazarov and S.I. Zavyalov [6]. In a 3-necked flask fitted with mechanical stirrer, dropping funnel and reflux condenser was prepared the potassium derivative of methyldihydroresorcinol from 9 g caustic potash in 40 ml water and 20 g methyldihydroresorcinol. Mixture was stirred at room temperature for 10 minutes and then 22 g 4-bromobutene-2 (b.p. 104-106°; n_D^{20} 1.4810 [18]) in 50 ml dioxane was added. The reaction mixture was stirred at 20° for 30 minutes and then for 1.5 hours on a boiling water bath (until disappearance of the alkaline solution). The mixture was cooled and extracted with ether. The ethereal extract was subsequently washed with hydrochloric acid (1:1), saturated soda solution, water and dried over sodium sulfate. The ether was driven off, the residue was vacuum-distilled and 7.5 g 2-methyl-2-crotylcyclohexane-1,3-dione (VI) was obtained with b.p. 100-100.5° at 2 mm; n_D^{21} 1.4878, d_4^{20} 1.0267, MR 50.58; calc. 50.35. Yield 27%

Found %: C 72.34, 72.40; H 8.77, 8.84. $C_{11}H_{16}O_2$. Calculated %: C 73.35; H 8.94.

When the condensation was carried out in a medium of anhydrous methanol under the conditions of the preparation of (IV), a product was obtained with b.p. 109.5-111°, n_D^{22} 1.4750, which was probably a mixture of (VI) with (VIIa). Attempts failed to effect the cyclization of Compound (VI) by means of heating it (at 120-160°) with phosphoric anhydride (0.5-10% of weight of taken diketone) for 4-8 hours.

Hydrogenation of 2-methyl-2-crotylcyclohexane-1,3-dione (VI). 3 g 2-methyl-2-crotylcyclohexane-1,3-dione in 20 ml alcohol was hydrogenated in the presence of platinum oxide. 400 ml hydrogen was absorbed in the course of 30 minutes (theoretically 393 ml, based on 1 mole). The catalyst was filtered off, the alcohol was driven off under a slight vacuum and the residue was distilled and yielded 2.5 g 2-methyl-2-butylcyclohexane-1,3-dione (VII) with b.p. 94-95° at 2 mm, n_D^{21} 1.4732.

Found %: C 72.51, 72.66; H 10.42, 10.42. $C_{11}H_{18}O_2$. Calculated %: C 72.48; H 9.95.

Condensation of 2-methylcyclohexane-1,3-dione with 1,3-dichlorobutene-2. In a 3-necked flask fitted with mechanical stirrer, reflux condenser, dropping funnel and thermometer was prepared the potassium derivative of 2-methylcyclohexane-1,3-dione from 14 g caustic potash in 60 ml water and 31.5 g 2-methylcyclohexane-1,3-dione. The solution was stirred at room temperature for 15 minutes, and then 33 g 1,3-dichlorobutene-2 in 60 ml dioxane was added. The reaction mass was heated for 2 hours on a water bath (until disappearance of the alkaline reaction), cooled and extracted with ether. The ethereal extract was washed several times with dilute (1:1) hydrochloric acid and then with saturated soda solution, with water and dried with magnesium sulfate. Fractionation yielded 18.6 g 2-methyl-2(γ-chlorocrotyl)-cyclohexane-1,3-dione (VIII) with b.p. 127-129° at 2.5 mm, n_D^{18} 1.5060, d_4^{20} 1.1476, MR 55.59; calc. 55.22. Yield 35%

Found %: C 61.31, 61.49; H 7.28, 7.38; Cl 16.48, 16.39. $C_{11}H_{15}O_2Cl$. Calc. %: C 61.53; H 7.04; Cl 16.52.

Attempts failed to effect the cyclization of this substance by heating it (120-160°) in vacuum (15-25 mm) with phosphoric anhydride.

Condensation of 2-methylcyclohexane-1,3-dione with 2-methyl-4-bromobutene-2. In a 3-necked flask fitted with mechanical stirrer, dropping funnel, thermometer and reflux condenser was prepared a solution of sodium methylate from 6.9 g sodium and 80 ml anhydrous methanol. To the cooled solution of sodium methylate was added 37.8 g 2-methylcyclohexane-1,3-dione (m.p. 207-208°) and the reaction mixture was heated for 15 minutes on a water bath at 70°. The mixture was then cooled and with vigorous stirring was added drop-wise 46 g 2-methyl-4-bromobutene-2 and the mixture heated up to 65°. The reaction mass was stirred for 2 hours at room temperature. The alcohol was driven off under a slight vacuum and to the residue was added 70 ml water and it was extracted with ether. The ethereal extract was washed 3 times with a saturated solution of soda and dried with potash. The ether was driven off and the residue was vacuum-distilled. Yield 39 g 2-methyl-2-(γ,γ-dimethylallyl)-cyclohexane-1,3-dione (IX) with b.p. 108-110° at 3 mm, n_D^{20} 1.4908. On standing the substance completely crystallized and melted at 40-41° (from n-hexane). Yield 67%.

Found %: C 74.35, 74.06; H 9.35, 9.25. $C_{12}H_{18}O_2$. Calculated %: C 74.18; H 9.33.

The substance gave no reaction with an alcoholic solution of ferric chloride and was not hydrolized by a dilute solution of hydrochloric acid. When this condensation was carried out in aqueous-dioxane medium [under conditions of preparation for 2-methyl-2-crotylcyclohexane-1,3-dione (VI)], the yield of 2-methyl-2-(γ,γ-dimethylallyl)-cyclohexane-1,3-dione (IX) fell to 33%.

Condensation of 2-methylcyclohexane-1,3-dione with 2-methyl-4-chlorobutene-2. The condensation was carried out in the manner described in the preceding experiment, starting from 5 g 2-methylcyclohexane-1,3-dione and 5.5 g 2-methyl-4-chlorobutene-2, but for completion of the reaction the mixture was heated for 2 hours at 70°. We obtained 2.7 g 2-methyl-2-(γ,γ-dimethylallyl)-cyclohexane-1,3-dione (IX) with b.p. 108-110° at 3 mm; m.p. 40°, n_D^{20} 1.4909. Yield 36%.

Cyclization of 2-methyl-2-(γ,γ-dimethylallyl)-cyclohexane-1,3-dione (IX). A mixture of 10 g 2-methyl-2-(γ,γ-dimethylallyl)-cyclohexane-1,3-dione (IX) and 0.6 g phosphoric anhydride was heated in vacuum (10 mm) at 116-120° for 1.5 hours; 0.6 g water separated out (0.9 g water can theoretically split out) and the refractive index increased from 1.4908 to 1.5290. The reaction mass was treated with saturated soda solution and the product was extracted with ether, dried with potash and, after driving off the ether, was vacuum-distilled: 1st fraction had b.p. 92-97° at 1 mm, n_D^{22} 1.5260 (2 g); the 2nd fraction had b.p. 97-100° at 1 mm, n_D^{22} 1.5280 (2 g); the 3rd fraction had b.p. 100-130° at 1 mm, n_D^{22} 1.5240 (1 g), residue 4 g.

The 1st and 2nd fraction crystallized at the time of distillation and the 3rd fraction did not crystallize at all. In all 3 g of crystalline ketone was obtained with m.p. 47-48° (yield 33%). A two-fold crystallization from n-hexane yielded 2.3 g pure 6,9-dimethyl-1-keto-$\Delta^{4(10),5}$-hexahydronaphthalene (XII) with m.p. 50-51°, $\lambda_{max.}$ (in isooctane) 252 mμ.

Found %: C 81.85, 81.70; H 9.20, 9.24. $C_{12}H_{16}O$. Calculated %: C 81.77; H 9.15.

A mixed sample with initial diketone (IX) gave a depression (it melted at 22-25°). The obtained 6,9-dimethyl-1-keto-$\Delta^{4(10),5}$-hexahydronaphthalene (XII) was very readily soluble in petroleum ether, alcohol, ether and less in n-hexane. Ketone (XII) was very unstable and upon standing for 2 days, was converted to a yellow oil from which the crystalline substance could no longer be obtained. Elementary analysis showed a decided decrease in carbon content (found %: C 79.46, 79.25; H 9.07, 9.11). This ketone could be stored in a nitrogen atmosphere with deep freezing (-70°). The unusual instability of ketone (XII) is due to its spatial structure and indicates the strain of such a diene configuration.

The semicarbazone of ketone (XII) was in the form of white crystals which had m.p. 193-194° (from alcohol) with decomposition.

Found %: N 18.38, 18.28. $C_{13}H_{19}N_3$. Calculated %: N 18.01.

The 2,4-dinitrophenylhydrazone had m.p. 137-138° from a mixture of alcohol and benzene 1:1, $\lambda_{max.}$ (in isooctane) 346 mμ.

Found %: N 15.91, 15.65. $C_{18}H_{20}O_4N_4$. Calculated %: N 15.72.

Upon being heated with pyridine butyrate at 130° in vacuum (10 mm) for 4 hours, 2-methyl-2-(γ,γ-dimethylallyl)-cyclohexane-1,3-dione did not cyclize and returned unchanged.

Reduction of 6,9-dimethyl-1-keto-$\Delta^{4(10),5}$-hexahydronaphthalene (XII), according to Kizhner. A mixture of 5 ml diethylene glycol, 1.6 g 6,9-dimethyl-1-keto-$\Delta^{4(10),5}$-hexahydronaphthalene (XII) (m.p. 50°), 1.5 ml hydrazine hydrate and 1.5 ml alcohol was heated on a water bath for 1 hour, and then to this was added sodium diethylene glycolate (prepared from 0.6 g metallic sodium in 10 ml diethylene glycol). In the course of 2 hours the temperature was raised from 120 to 190° and the low-boiling fraction slowly was driven off. The mixture was heated at 190-205° for 6 hours more. The whole operation was carried out in a stream of nitrogen. On completion of heating, the reaction mass and distillate were treated with 20 ml water and extracted with ether. The combined ethereal extracts were washed twice with 18% hydrochloric acid and once with a solution of potash and dried with potash. The ether was driven off and the residue was vacuum-distilled in a stream of nitrogen over metallic sodium. Yield 1 g of 6,9-dimethyl-$\Delta^{4(10),5}$-hexahydronaphthalene (XIII) with b.p. 107.5-108° at 15 mm, n_D^{20} 1.5048.

Dehydrogenation of 6,9-dimethyl-$\Delta^{4(10),5}$-hexahydronaphthalene (XIII). A solution of 1 g 6,9-dimethyl-$\Delta^{4(10),5}$-hexahydronaphthalene in 15 ml dry benzene and 0.5 g 10% palladized charcoal was heated in a rotary autoclave in an atmosphere of nitrogen for 21 hours at 360-370°. The catalyst was filtered off and the solvent was driven off in vacuum. The residue yielded 0.65 g liquid (n_D^{20} 1.5650), which upon distillation yielded 0.23 g of substance with b.p. 117-118° at 18 mm (n_D^{20} 1.5750), from which a picrate was prepared with m.p. 114-115°. The literature on the picrate of β-methylnaphthalene gives m.p. 115° [9]. A mixed sample with a known specimen of the picrate of β-methylnaphthalene gave no depression (it melted at 114-115°).

Condensation of maleic anhydride with 6,9-dimethyl-1-keto-$\Delta^{4,5}$-hexahydronaphthalene (XII). 1 g 6,9-dimethyl-1-keto-$\Delta^{4,5}$-hexahydronaphthalene (XII), 0.5568 g maleic anhydride and 6 ml anhydrous benzene were heated for 4.5 hours in a metal ampul at 200° in presence of traces of pyrogallol. The benzene was driven off, the residue was dissolved in 2 ml acetone and set aside to crystallize. After several days, 0.54 g of crystals came down with m.p. 140-145°. After recrystallization from a mixture of acetone and n-heptane (1:3), 0.36 g adduct (XIV) was obtained with m.p. 159-160°. Yield 35%.

Found %: C 69.68, 69.65; H 6.81, 6.62. $C_{16}H_{18}O_4$. Calculated %: C 69.95; H 6.60.

When 6,9-dimethyl-1-keto-$\Delta^{4(10),5}$-hexahydronaphthalene was reacted with maleic anhydride at room temperature (for 3 days) and also with heating (170°, 3 hours), the initial 6,9-dimethyl-1-keto-$\Delta^{4(10),5}$-hexahydronaphthalene was returned.

Hydrolysis of anhydride (XIV) with 5% caustic soda solution (100°, 2 hours) yielded the corresponding acid, which upon being heated above 100°, was converted to the initial anhydride.

Preparation of enol acetate of methyldihydroresorcinol. A mixture of 20 g methyldihydroresorcinol (m.p. 205-206°) and 80 g acetic anhydride was heated for 2 hours at 100°. The excess of acetic anhydride was driven off and the residue was driven off in vacuum: the 1st fraction had b.p. 56-87° at 1 mm, n_D^{20} 1.4750 (3 g); the 2nd fraction had b.p. 87-89° at 1 mm, n_D^{20} 1.4895 (20.5 g).

The 2nd fraction was pure enol acetate of methyldihydroresorcinol, b.p. 88-89° at 1 mm, n_D^{20} 1.4895, d_4^{20} 1.1067. Yield 76%.

Found %: C 64.21, 64.31; H 7.01, 7.13. $C_9H_{12}O_3$. Calculated %: C 64.26; H 7.19.

The substance readily hydrolyzed even at room temperature in acid (with 8% hydrochloric acid) as well as in alkaline mediums (in 10% caustic soda solution), giving initial methyldihydroresorcinol.

Reaction of enol acetate of methyldihydroresorcinol with methylmagnesium iodide. In a 3-necked flask fitted with mechanical stirrer, dropping funnel and reflux condenser was prepared a solution of methylmagnesium iodide, starting from 6.4 g magnesium, 40 g methyl iodide and 200 ml absolute ether. To a solution of methylmagnesium iodide was added 11.4 g enol acetate of methyldihydroresorcinol in 50 ml absolute ether in the course of 40 minutes and the reaction mixture was heated for 2 hours at 35-40°. The product was treated with 50 ml hydrochloric acid (1:1), extracted with ether, washed with water, with a solution of sodium hyposulfite, again with water, dried with magnesium sulfate and vacuum-distilled. Yield 3.5 g of 2,3-dimethyl-Δ^2-cyclohexen-1-one (XV) with b.p. 78-78.5° at 8 mm, n_D^{20} 1.4995, d_4^{20} 0.9695. Yield 41%.

Treatment of the reaction mass with water or with ammonium chloride also yields 2,3-dimethyl-Δ^2-cyclohexen-1-one, the semicarbazone of which had m.p. 228-230° (from alcohol) with decomposition. According to the literature data, the semicarbazone had m.p. 225° (with decomp.) [19].

Found %: C 59.60, 59.75; H 8.47, 8.50; N 23.23, 23.14. $C_9H_{15}ON_3$. Calculated %: C 59.65; H 8.34; N 23.18.

2,4-Dinotrophenylhydrazone had m.p. 170° (from alcohol).

Found %: C 55.20, 55.02; H 5.15, 5.36; N 18.09, 18.06. $C_{14}H_{16}O_4N_4$. Calculated %: C 55.25; H 5.18; N 18.41.

Hydrogenation of 2,3-dimethyl-Δ^2-cyclohexen-1-one. 2.25 g 2,3-dimethyl-Δ^2-cyclohexen-1-one in 10 ml alcohol was hydrogenated in presence of platinum oxide. 426 ml hydrogen was absorbed in the course of 23 hours (theoretically 405 ml, based on 1 mole). The solvent was driven off, the residue was vacuum-distilled. Yield 1.4 g 2,3-dimethylcyclohexan-1-one with b.p. 63-63.5° at 15 mm, n_D^{20} 1.4510.

The semicarbazone had m.p. 201-202° (from alcohol).

Found %: N 22.99, 22.88. $C_9H_{17}ON_3$. Calculated %: N 22.93.

According to the literature data, the semicarbazone of 2,3-dimethylcyclohexan-1-one has m.p. 203-204° [19].

SUMMARY

A study was made of the condensation of allylic halo-derivatives (2-methyl-4-bromobutene-2, 2-methyl-4-chlorobutene-2, crotyl bromide and 1,3-dichlorobutene-2) with acetoacetic ester, methylacetoacetic ester, dihydroresorcinol and methyldihydroresorcinol, and the corresponding substituted acetoacetic esters, dihydroresorcinols and methyldihydroresorcinols (I-IX) were obtained. With the help of phosphorus pentoxide, intramolecular condensation (with loss of water) was effected of 2-methyl-2-(γ,γ-dimethylallyl)-cyclohexane-1,3-dione (IX) to 6,9-dimethyl-1-keto-$\Delta^{4(10),5}$-hexahydronaphthalene (XII), whose structure was verified by reduction and dehydrogenation to 2-methylnaphthalene and by a series of other transformations. Under similar conditions 2-(γ,γ-dimethylallyl)-cyclohexane-1,3-dione (IV) was cyclized to 2,2-dimethyltetrahydrochroman-5-one (X) in 77% yield. The substituted cyclohexane-1,3-diones (VI) and (VIII), containing crotyl radicals, were found to be incapable of cyclization, probably due to their spatial structure (trans-arrangement of the methyl groups of the side chain in relation to the carbonyl of the cyclohexane ring).

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HETEROCYCLIC COMPOUNDS

37. SYNTHESIS OF HETEROCYCLIC AMINOALCOHOLS AND THEIR ESTERS

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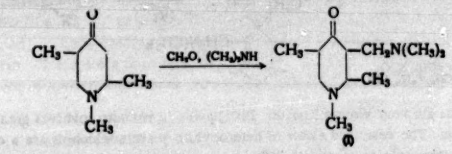
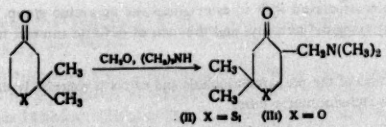
In the preceding communication we described the synthesis of a series of heterocyclic β-aminoketones by the Mannich reaction. From these heterocyclic β-aminoketones we can pass, by reduction or by condensation at the carbonyl group, to secondary or tertiary heterocyclic γ-aminoalcohols respectively. By subsequent esterification with various organic acids one can then obtain a new series of esters for pharmacological investigation.

Many esters of secondary and tertiary γ-aminoalcohols of the aliphatic and alicyclic series exhibit physiological activity to various extents, and the synthesis of such esters accordingly has a definite pharmacological value [1-5]. Also well known is the high anesthetic activity of some esters of γ-piperidols synthesized in our laboratory and by other authors [6-8].

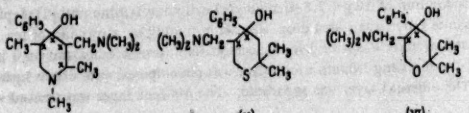
The heterocyclic β-aminomethyl-γ-ketones 1,2,5-trimethyl-3-(dimethylaminomethyl)-4-piperidone (I), 2,2-dimethyl-5-(dimethylaminomethyl)-tetrahydrothiopyran-4-one (II) and 2,2-dimethyl-5-(dimethylaminomethyl)-tetrahydropyran-4-one (III) were obtained by us by aminomethylation (Mannich reaction) of the corresponding heterocyclic γ-ketones with the help of formaldehyde and dimethylamine.





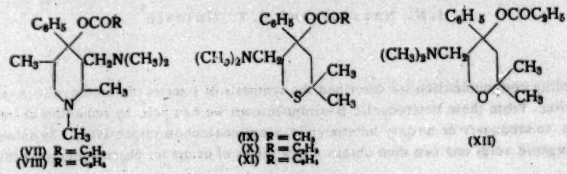
(II) X = S; (III) X = O

By condensation with phenyllithium and phenyl magnesium bromide (taken in 50% over the theoretical amount), the above heterocyclic β-aminomethyl-γ-ketones (I, II and III) were transformed into the corresponding tertiary γ-aminoalcohols: 1,2,5-trimethyl-3-(dimethylaminomethyl)-4-phenyl-4-piperidol (IV) (yield 61% with phenyllithium), 2,2-dimethyl-5-(dimethylaminomethyl)-4-phenyltetrahydrothiopyran-4-ol (V) (yield 63% with phenyllithium) and 2,2-dimethyl-5-(dimethylaminomethyl)-4-phenyltetrahydropyran-4-ol (VI) (yield 34.5% with phenyl magnesium bromide).

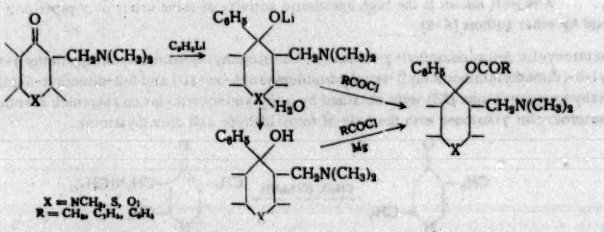


The prepared phenylated γ-aminoalcohols (IV, V and VI) are viscous liquids distilling in vacuum without decomposition and stable when kept. They are all mixtures of stereoisomers, due to the presence in the piperidinic γ-aminoalcohol (IV) of four asymmetric, and in the two other alcohols (V) and (VI) of two asymmetric, carbon atoms (marked with crosses in the formulas).

From the work of our laboratory [8] and of other investigators [6,7,9] it is known that heterocyclic tertiary alcohols sometimes do not readily undergo esterification. The best results were obtained by the action of chlorides of organic acids on the lithium alcoholates of 4-phenyl-4-piperidols formed by reaction of phenyllithium with 4-piperidones, and also by the action of the acid chlorides on the free alcohols in benzene solution in presence of metallic magnesium [10]. Applying both these methods to the esterification of the prepared heterocyclic γ-aminoalcohols (IV, V and VI), we synthesized the following esters: the propionate (VII) and benzoate (VIII) of 1,2,5-trimethyl-3-(dimethylaminomethyl)-4-phenyl-4-piperidol; the acetate (IX), the propionate (X) and the benzoate (XI) of 2,2-dimethyl-5-(dimethylaminomethyl)-4-phenyltetrahydrothiopyran-4-ol, and also the propionate (XII) of 2,2-dimethyl-5-(dimethylaminomethyl)-4-phenyl-tetrahydropyran-4-ol.



The entire course of the transformation may be represented in the following general scheme:



The synthesized esters are very viscous liquids. Distillation in vacuum involves great difficulties and the possibility of decomposition. The described esters of heterocyclic γ-aminoalcohols are a compietely new type of compound in which a heterocycle is associated with an ester group and an amino group. Such compounds may be expected to possess distinctive physiological activity, and they are of definite interest from the pharmacological viewpoint.

Isolation of crystalline derivatives of the prepared alcohols and esters is extremely difficult, due to the fact that they are mixtures of various stereoisomeric forms.

EXPERIMENTAL

1,2,5-Trimethyl-3-(dimethylaminomethyl)-4-phenyl-4-piperidol (IV). In a 3-necked flask fitted with mercury-sealed stirrer, dropping funnel, nitrogen lead tube and reflux condenser with calcium chloride tube was placed 15 ml absolute ether and 1 g fine lithium filings. Upon stirring, a solution of 12.5 g bromobenzene in 15 ml absolute ether was added. The mixture was then heated for 1 hour while the ether boiled. The reaction was carried out in an atmosphere of dry nitrogen until complete solution of the lithium. To the phenyllithium, prepared in this manner, a solution of 10 g 1,2,5-trimethyl-3-(dimethylaminomethyl)-4-piperidone (I) [b.p. 84-89° (4 mm)] in 20 ml absolute ether was added drop-wise with cooling, by a mixture of ice and salt (-10°), and vigorous stirring. The reaction mass was stirred for 5 hours at room temperature and for 1 hour while the ether boiled. On the next day, the resulting lithium alcoholate was decomposed with dilute hydrochloric acid (1:1) with ice-water cooling. The ethereal layer was separated. The aqueous layer was treated with ether to com-

pletely remove neutral products and was then neutralized with soda and, in presence of ether with external water cooling, it was saturated with caustic soda. The basic products were extracted repeatedly with ether and after passage of a stream of carbon dioxide and drying with sodium sulfate, they were vacuum-fractionated. Yield 8.5 g (61%) 1,2,5-trimethyl-3-(dimethylaminomethyl)-4-phenyl-4-piperidol (IV) in the form of a very viscous yellowish liquid with an amine odor. B.p. 150-154° (1 mm), n_D^{20} 1.5246.

Found %: C 73.64, 73.60; H 9.70, 9.40; N 9.98, 10.02. $C_{17}H_{28}ON_2$. Calculated %: C 73.86; H 10.21; N 10.14.

Besides this, 1.5 g of initial β-aminomethyl-γ-piperidone (I), b.p. 70-76° (1 mm), n_D^{20} 1.4741, was returned from the reaction. There remained 2 g of resinous residue after fractionation.

After recrystallization from alcohol, the picrate of phenylpiperidol (IV) had m.p. 87-88°.

Found %: N 13.94, 13.96. $C_{23}H_{31}O_9N_5$. Calculated %: N 13.86.

2,2-Dimethyl-5-(dimethylaminomethyl)-4-phenyltetrahydrothiopyran-4-ol (V). To a solution of phenyllithium, prepared from 1 g metallic lithium and 13 g bromobenzene in 80 ml absolute ether was added drop-wise a solution of 10 g 2,2-dimethyl-5-(dimethylaminomethyl)-tetrahydrothiopyran-4-one (II) (b.p. 99-101° at 4 mm) in 20 ml absolute ether with vigorous stirring and cooling (mixture of ice and salt). The reaction mixture was stirred for 5 hours at room temperature and 2 hours more while the ether boiled. The next day the product, upon cooling with ice water, was hydrolyzed with 15% hydrochloric acid (cooling with ice water). Further treatment was the same as in the preceding experiment. Yield 8.7 g (63%) 2,2-dimethyl-5-(dimethylaminomethyl)-4-phenyltetrahydrothiopyran-4-ol (V) in the form of a very viscous yellowish liquid. B.p. 145-150° (1 mm).

Found %: C 69.53, 69.40; H 8.90, 8.68; N 4.88, 4.85. $C_{16}H_{25}ONS$. Calculated %: C 68.77; H 9.02; N 5.01.

The picrate of phenylthiopyranol had m.p. 190-191° (from alcohol).

Found %: N 11.16, 10.89. $C_{22}H_{28}O_9N_4S$. Calculated %: N 11.02.

2,2-Dimethyl-5-(dimethylaminomethyl)-4-phenyltetrahydropyran-4-ol (VI). To a solution of phenylmagnesium bromide, prepared from 1.8 g magnesium and 12.5 g bromobenzene in 20 ml absolute ether was added drop-wise with vigorous stirring and ice-water cooling a solution of 9 g 2,2-dimethyl-5-(dimethylaminomethyl)-tetrahydropyran-4-one (III) (b.p. 83-86° at 4 mm) in 15 ml absolute ether. The reaction mass was stirred for 2 hours while the ether boiled; upon cooling with ice water, it was decomposed with 15% hydrochloric acid and treated in the usual manner. Yield 4.4 g (34.5%) 2,2-dimethyl-5-(dimethylaminomethyl)-4-phenyltetrahydropyran-4-ol (VI) in the form of a viscous yellowish liquid. B.p. 126-133° (1 mm).

Found %: C 72.18, 72.53; H 9.22, 9.56; N 5.23, 5.21. $C_{16}H_{25}O_2N$. Calculated %: C 72.96; H 9.57; N 5.32.

3 g initial β-aminomethyl-γ-pyrone (III) (b.p. 61-65°, 1 mm) was returned from the reaction. After fractionation, there was 2.5 g resinous residue.

Propionate of 1,2,5-trimethyl-3-(dimethylaminomethyl)-4-phenyl-4-piperidol (VII). a) A solution of 2.8 g phenylpiperidol (IV) in 3 ml dry benzene was heated at 90° with 5 ml propionyl chloride in presence of 0.12 g fine magnesium filings for 10 hours. The next day, the hard brown vitreous mass was rubbed to a powder under a layer of absolute ether and multiple treatments with absolute ether removed a considerable portion of the resinous substances and yielded a purer product. The precipitate, containing magnesium, was then dissolved in a small quantity of water, the free base was liberated with soda (in presence of ether with external cooling with cold water) and repeatedly extracted with ether. After drying with sodium sulfate, the ethereal solution was carefully filtered and the ether was driven off. The residue, which was a colorless viscous oil, was held for a long period in a vacuum-desiccator over calcium chloride. Yield 2 g of propionate of 1,2,5-trimethyl-3-(dimethylaminomethyl)-4-phenyl-4-piperidol (VII).

Found %: N 8.30, 8.12. $C_{20}H_{32}O_2N_2$. Calculated %: N 8.43.

b) To a solution of phenyllithium, prepared from 1 g lithium and 13 g bromobenzene in 80 ml absolute ether with vigorous stirring and cooling (ice-salt mixture, -10°) was added drop-wise a solution of 10 g 1,2,5-trimethyl-3-(dimethylaminomethyl)-4-piperidone (I) in 20 ml absolute ether. The reaction mass was stirred for 5 hours at room temperature and for 1 hour while the ether boiled and was set aside overnight. To the lithium

alcoholate of phenylpiperidol (IV), prepared in this manner, with ice-water cooling was added drop-wise 26 ml propionyl chloride, dissolved in an equal volume of absolute ether. The mixture was stirred for 3 hours at room temperature and for 5 hours while the ether boiled. On the next day pieces of ice were added to the reaction mass while cooling with ice water and then water was run in until complete solution of the precipitate. The ethereal layer was separated, the aqueous layer was treated with ether to remove the neutral products and was saturated with soda (in presence of ether and with cooling). The base was repeatedly extracted with ether and dried with sodium sulfate. Into the carefully filtered ethereal solution of the base was passed a stream of dry hydrogen chloride. The flakes of hydrochloride of the propionate of 1,2,5-trimethyl-3-(dimethylaminomethyl)-4-phenyl-4-piperidol (VII) which separated out could be preserved only under a layer of absolute ether or in a desiccator over drying agents. It quickly deliquesced to an oil in air. We failed to obtain the hydrochloride in a stable crystalline state.

Benzoate of 1,2,5-trimethyl-3-(dimethylaminomethyl)-4-phenyl-4-piperidol (VIII). a) A solution of 2.8 g phenylpiperidol (IV) in 3 ml benzene was heated at 90° with 7 ml benzoyl chloride in presence of 0.12 g magnesium filings for 10 hours. On the next day the hard vitreous brown mass was treated in the same manner as in the preparation of the propionate of this piperidol. Yield about 2.5 g benzoate of 1,2,5-trimethyl-3-(dimethylaminomethyl)-4-phenyl-4-piperidol (VIII) in the form of a viscous oil which did not crystallize upon long standing and upon freezing was converted to a vitreous mass.

Found %: C 74.52, 74.71; H 8.07, 8.21; N 7.51, 7.04. $C_{24}H_{32}O_2N_2$. Calculated %: C 75.76; H 8.48; N 7.36.

b) To the lithium alcoholate of phenylpiperidol (IV), prepared from 1 g lithium, 13 g bromobenzene and 10 g aminopiperidone (I) in 100 ml absolute ether, as described in the preparation of the propionate of this piperidol, with ice-water cooling was added drop-wise 35 ml of benzoyl chloride, dissolved in an equal volume of absolute ether. The reaction mixture was stirred for 2 hours at room temperature and then for 6 hours while the ether boiled. Further treatment of the mixture was as in the preparation of the propionate. Into the ethereal solution of the prepared benzoate of 1,2,5-trimethyl-3-(dimethylaminomethyl)-4-phenyl-4-piperidol (VIII) was passed dry hydrogen chloride until saturation. We failed to obtain the hydrochloride which separated out in a crystalline form.

Acetate of 2,2-dimethyl-5-(dimethylaminomethyl)-4-phenyltetrahydrothiopyran-4-ol (IX). A solution of 2.8 g phenylthiopyranol (V) in 3 ml benzene was heated at 90° with 3 ml acetyl chloride in presence of 0.12 g magnesium filings for 5 hours. The treatment was carried out as in the preparation of propionate (VII). The residue was a viscous oil which was the acetate of 2,2-dimethyl-5-(dimethylaminomethyl)-4-phenyltetrahydrothiopyran-4-ol (IX).

Found %: C 66.36; 66.63; H 8.11, 8.31. $C_{18}H_{27}O_2NS$. Calculated %: C 67.25; H 8.47.

Propionate of 2,2-dimethyl-5-(dimethylaminomethyl)-4-phenyltetrahydrothiopyran-4-ol (X). a) A solution of 2.8 g phenylthiopyranol (V) in 3 ml benzene was heated at 90° with 3.5 ml propionyl chloride in presence of 0.12 g magnesium filings for 5 hours. Next day the reaction mass was treated in the same manner as in the preceding experiment. After driving off the ether, the residue was in the form of a viscous oil with the characteristic odor of thio compounds and was the propionate of 2,2-dimethyl-5-(dimethylaminomethyl)-4-phenyltetrahydrothiopyran-4-ol (X).

Found %: C 68.51, 68.92; H 7.73, 7.40; N 3.99, 4.14. $C_{19}H_{29}O_2NS$. Calculated %: C 68.02; H 8.71; N 4.18.

b) To a solution of phenyllithium, prepared from 1 g lithium and 13 g bromobenzene in 80 ml absolute ether, with cooling (ice-salt mixture) and vigorous stirring was added drop-wise a solution of 10 g 2,2-dimethyl-5-(dimethylaminomethyl)-tetrahydrothiopyran-4-one (II) in 20 ml absolute ether. The reaction mixture was stirred for 3 hours at room temperature and for 2 hours more while the ether boiled. To the lithium alcoholate of 2,2-dimethyl-5-(dimethylaminomethyl)-4-phenyltetrahydrothiopyran-4-ol (V), prepared in this manner, with ice-water cooling was added drop-wise 26 ml propionyl chloride, dissolved in an equal volume of absolute ether and the mixture was stirred for 2 hours at room temperature and for 5 hours while the ether boiled. On the next day pieces of ice were added to the reaction mass with external ice-water cooling and then water was added until the precipitate dissolved. The ethereal layer was separated, the aqueous layer was treated with ether to remove neutral products and was saturated with soda (with cooling and in presence of ether). The base was repeatedly extracted with ether and dried with sodium sulfate. Into the carefully filtered ethereal solution of the

base was passed a stream of dry hydrogen chloride and the oily hydrochloride of the propionate of 2,2-dimethyl-5-(dimethylaminomethyl)-4-phenyltetrahydrothiopyran-4-ol (X) that separated out was rubbed to a powder under a layer of absolute ether. It was very hygroscopic and again deliquesced to an oil in air. In spite of all our efforts, we could not isolate the hydrochloride in a stable crystalline form.

Benzoate of 2,2-dimethyl-5-(dimethylaminomethyl)-4-phenyltetrahydrothiopyran-4-ol (XI). a) A solution of 2.8 g phenylthiopyranol (V) in 3 ml benzene was heated at 90° with 5 ml benzoyl chloride in presence of 0.12 g fine magnesium filings for 5 hours. On the next day the reaction mass was treated the same way as in the similar preceding experiments. After driving off the ether, the residue was in the form of a viscous oil with the odor of a thio compound and was the benzoate of 2,2-dimethyl-5-(dimethylaminomethyl)-4-phenyltetrahydrothiopyran-4-ol (XI).

Found %: C 71.38, 71.94; H 7.46, 7.30; N 3.41, 3.53. $C_{23}H_{29}O_2NS$. Calculated %: C 72.03; H 7.62; N 3.65.

b) To the lithium alcoholate of 2,2-dimethyl-5-(dimethylaminomethyl)-4-phenyltetrahydrothiopyran-4-ol (V), prepared as described above from 1 g lithium, 13 g bromobenzene and 10 g 2,2-dimethyl-5-(dimethylaminomethyl)-tetrahydrothiopyran-4-one (II) in 100 ml absolute ether, with ice-water cooling, was added dropwise 35 ml benzoyl chloride, dissolved in an equal volume of absolute ether. The mixture was stirred for 2 hours at room temperature and 5 hours while the ether boiled. Further treatment of the reaction mixture was carried out in the same manner as in the preparation of the propionate of this thiopyranol. When a stream of dry hydrogen chloride was passed into the ethereal solution of the benzoate base, a voluminous flocculent precipitate came down and was separated and washed on a filter with absolute ether. The obtained friable precipitate was very hygroscopic and rapidly deliquesced to an oil in air. After drying in a vacuum-desiccator over caustic potash, the dry spongy mass was dissolved in anhydrous alcohol and boiled with activated charcoal until almost complete decolorization of the solution. The alcoholic solution was partially evaporated in vacuum and then, after long standing and periodic addition of dry acetone, until the solution became turbid, the crystalline hydrochloride of the benzoate of 2,2-dimethyl-5-(dimethylaminomethyl)-4-phenyltetrahydrothiopyran-4-ol (XI) came down in the form of a fine powder with m.p. 189-190°. The hydrochloride was readily soluble in water, methanol, alcohol, and was insoluble in acetone.

Found %: Cl 8.22, 8.51. $C_{23}H_{30}O_2NClS$. Calculated %: Cl 8.44.

After separation of the hydrochloride crystals from the mother liquor, acetone and alcohol were driven off. The residue was dissolved in water, decomposed with soda and the base was extracted with ether and dried with sodium sulfate. The ethereal solution was carefully filtered and the ether was driven off. The residue was a viscous oil of the base of benzoate of 2,2-dimethyl-5-(dimethylaminomethyl)-4-phenyltetrahydrothiopyran-4-ol (XI).

Propionate of 2,2-dimethyl-5-(dimethylaminomethyl)-4-phenyltetrahydropyran-4-ol (XII). A solution of 2.6 g phenylpyranol (VI) in 3 ml benzene was heated at 90° with 3.5 ml propionyl chloride in presence of 0.12 g magnesium filings for 5 hours. Separation was carried out by the previously described method. The separated viscous oil was the propionate of 2,2-dimethyl-5-(dimethylaminomethyl)-4-phenyltetrahydropyran-4-ol (XII).

Found %: C 70.29, 70.15; H 8.44, 8.76; N 4.55, 4.85. $C_{19}H_{29}O_3N$. Calculated %: C 71.44; H 8.15; N 4.38.

Into a solution of the propionate base in absolute ether was passed dry hydrogen chloride until it was saturated. The hydrochloride which separated out could not be crystallized.

SUMMARY

Three heterocyclic tertiary γ-aminoalcohols (IV, V, VI) were synthesized by interaction of organomagnesium and organolithium compounds with the corresponding heterocyclic β-aminomethyl-γ-ketones. Treatment of these heterocyclic γ-aminoalcohols (or their lithium alcoholates) with organic acid chlorides led to formation of six esters (VII-XII) with the objective of their pharmacological investigation.

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THE PROBLEM OF THE REACTIVITY OF DIALKYLAMINOMETHYL ALKYL ETHERS AND OF COMPOUNDS OF SIMILAR STRUCTURE

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Introduction into an organic molecule (R'H) containing reactive hydrogen of the dialkylaminomethyl group can be effected with the help of various reactions:

$$R'H + R_2NH + CH_2O \rightarrow R'CH_2NR_2 + H_2O, \quad (1)$$

$$R'H + R_2NCH_2NR_2 \rightarrow R'CH_2NR_2 + R_2NH, \quad (2)$$

$$R'H + R_2NCH_2OR \rightarrow R'CH_2NR_2 + ROH. \quad (3)$$

The mechanism of these reactions is obscure. Cromwell [1] suggested that R_2NCH_2OR is the intermediate product when Reaction (1) is conducted in an alcoholic medium. Lieberman and Wagner [2], as well as a number of other authors [3], considered the intermediate formation of bis-(dialkylamino)-methylene and of dialkylaminomethanol to be possible in Reaction (1).

The structure of various dialkylaminomethylated substances – dialkylaminomethylalkyl ethers R_2NCH_2OR (I), bis-(dialkylamino)-methylenes $R_2NCH_2NR_2$ (II), and the conjectured intermediate product of Reaction (1), R_2NCH_2OH – may be represented by the general formula R_2NCH_2X, where X = NR_2, OR or OH. It may be suggested that in compounds of this type the polarization tendency of the C–X bond must be greater in the case of the unsymmetrical structure R_2NCH_2X in which the carbon of the methylene group is subjected to the polarizing influence of various radicals. Hence it follows that compounds with unsymmetrical structure of the type of dialkylaminomethyl alkyl ethers must be more reactive in nucleophilic substitutions than symmetrical compounds, such as bis-(dialkylamino)-methylene.

G. and R. Robinson [4] showed that dialkylaminomethyl alkyl esters readily form tertiary amines under the action of organomagnesium compounds. On the basis of these authors' work, we considered it would be of interest to approach the problem of the reactivity of compounds of the type of R_2NCH_2X by studying the action of phenyl magnesium bromide on the one hand on diethylaminomethyl ethyl ether and diethylaminomethylnonyl sulfide, and, on the other hand, on bis-(diethylamino)-methylene and bis-(piperidino)-methylene. The degree of reactivity can be judged from the amount of tertiary amine formed. In all cases the experiments were conducted under identical conditions.

It was found, in agreement with the data of [4] that diethylaminomethyl ethyl ether reacted very violently with C_6H_5MgBr and under the chosen experimental conditions N-benzyldiethylamine was isolated in 95% yield. The same was true of the reaction with diethylaminomethylnonyl sulfide (yield of N-benzyldiethylamine up to 90.8% and that of nonyl mercaptan 97.5%).

In contrast to the above compounds, reaction of C_6H_5MgBr with bis-(diethylamino)-methylene did not yield any N-benzyldiethylamine, while in the reaction with bis-(piperidino)-methylene the yield of N-benzylpiperidine was about 6%.

Higher reactivity might be expected in the case of bis-(dialkylamino)-methylenes containing alkyl residues at the nitrogen atom. These compounds are not described in the literature. It seemed that one method for their preparation might be the replacement of the alkoxy group in ethers (I) by the residue of a secondary amine. With this objective, a mixture of diethylaminomethyl ethyl ether (III) and piperidine (equimolar amounts) was heated at a temperature at which the low-boiling reaction products distilled off (100-110° in the mass). The

distillate was found to contain ethyl alcohol (60.6%) and diethylamine (29%). Although the formation of ethyl alcohol indicated that the reaction had gone in the desired direction, we did not succeed in isolating from the reaction mixture the anticipated unsymmetrical methylene $C_5H_{10}NCH_2N(C_2H_5)_2$. After numerous distillations we obtained the original Compound (III) (13%), bis-(piperidino)-methylene (80% reckoned on the piperidine taken) and a number of intermediate fractions without a sharp boiling point. The same results were obtained in experiments with excess of (3), i.e., under conditions favoring replacement of only the ethoxy group of the ether.

We know from the work of Snyder and co-workers [5] and of A.P. Terentyev and co-workers [6] that in a series of compounds the dialkylamino group can easily be replaced by the residue of a higher boiling secondary amine. We therefore attempted to obtain the unsymmetrical bis-aminomethylene by replacing one diethylamino group in bis-(diethylamino)-methylene by a piperidine residue. Diethylamine was actually separated in 83% yield from the distillate after heating equimolar amounts of bis-(diethylamino)-methylene and piperidine. However, as in reactions with (III), the reaction mass was a complex mixture from which we were able to isolate only bis-(piperidino)-methylene (56.2%), while the remaining fractions did not have sharp boiling points. The inability to obtain unsymmetrical aminomethylenes may have been due to the fact that during heating (both during the reaction and during fractional distillation) the originally formed unsymmetrical bis-aminomethylene rearranges to a symmetrical aminomethylene, in a similar manner to the rearrangement of unsymmetrical acetals which has frequently been observed by D.N. Kursanov, V.N. Setkina and V.M. Rodionov [7], and M.F. Shostakovsky and co-workers [8]. No success attended an attempt to fractionate the reaction products not by rectification but in the form of double compounds of bis-(dialkylamino)-methylenes with carbon bisulfide [9].

After failing to obtain unsymmetrical bis-(dialkylamino)-methylenes, we made use of compounds of related type: N-(diethylaminomethyl)-carbazole,

$$C_{12}H_8NCH_2N(C_2H_5)_2 \quad (IV)$$

and N-(piperidinomethyl)-carbazole

$$C_{12}H_8NCH_2C_5H_{10} \quad (V).$$

Reaction of C_6H_5MgBr with (IV) gave N-benzyldiethylamine in 93.2% yield and carbazole in 98.2% yield; reaction with (V) gave N-benzylpiperidine (93.6%) and carbazole (99.3%). Although Compounds (IV) and (V) contain the atomic grouping $>N-CH_2-N<$ typical of bis-(dialkylamino)-methylenes, the character of the nitrogen in the dibenzpyryl residue differs considerably from that of the nitrogen in the dialkylamino group. For this reason the high reactivity of (IV) and (V) can only to a certain extent reflect the suggested high reactivity of unsymmetrical bis-(dialkylamino)-methylenes in comparison with symmetrical compounds.

EXPERIMENTAL

The reaction of R_2NCH_2X with C_6H_5MgBr was carried out under the same conditions in all cases. An excess of C_6H_5MgBr was used for the reaction and 0.05 mole of investigated substance. A typical description of the experiment with diethylaminomethylnonyl sulfide is given below.

Reaction of phenylmagnesium bromide with diethylaminomethylnonyl sulfide (VI). To a cooled (to -8°) ethereal solution of C_6H_5MgBr, prepared from 3.6 g magnesium and 19.0 g bromobenzene in 80 ml ether, was added a solution of 12.25 g (VI) with b.p. 153-154° (6 mm) in 40 ml ether. With external cooling and regulation of the rate of addition of (VI) the temperature of the reaction mixture was held in the range 0 to +2°. Upon completion of adding (VI), the mixture was heated in the course of 30 minutes to 35° and boiled for 2.5 hours. The mixture was cooled to -10°, decomposed with 75 ml 10% HCl, the ethereal layer was separated and it was washed with dilute HCl. The hydrochloric acid solution of the amine was treated with concentrated ammonia solution and the base which separated out was extracted with ether. The extract was dried, the solvent was evaporated off and the remaining oil was vacuum-distilled. Yield 7.4 g (90.8%) of N-benzyldiethylamine with b.p. 93° (12 mm) and 210-212.5° (747 mm) [10]. The picrate had m.p. 121-121.6° (from C_2H_5OH). For identification, the picrate of N-benzyldiethylamine was prepared and was synthesized by Titov's method [10] and had m.p. 121-122°. A mixing test gave no depression. The ethereal extract, separated from the acid layer, was dried, steamed down and the residue was vacuum-distilled twice. Yield 7.8 g (97.5%) nonyl mercaptan with b.p. 98-100° (15 mm) [11]. From the residue of the distillation of the nonylmercaptan, crystallization from alcohol yielded diphenyl.

The results of the reaction of C_6H_5MgBr with other compounds and the properties of the obtained tertiary amine are given in the table.

Starting substance	Obtained tertiary amine	Yield (in %)	Boiling point	Content of N (in %) found	Content of N (in %) calc.	Melting point of picrate
Diethylaminomethyl-ethyl ether	$C_2H_5CH_2N(C_2H_5)_2$	95.0	210—212.5° (747 mm)	8.54	8.58	121—121.6°
Bis-piperidinomethyl-ene	$C_5H_{10}CH_2NC_5H_{10}$	6.0				178—179.5
N-(Diethylamino-methyl)-carbazole	$C_6H_4CH_2N(C_2H_5)_2$	93.2	210—212.5 (747 mm)	8.55	8.58	121—121.6
N-(Piperidinomethyl)-carbazole	$C_6H_4CH_2NC_5H_{10}$	93.6	119—121 (13 mm)	7.87	7.99	179—180.5

SUMMARY

A study was made of the relative reactivity of symmetrical and unsymmetrical dialkylaminomethylated substances with the help of their interaction with phenylmagnesium bromide.

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TAUTOMERIC COMPOUNDS

XX. THE MOBILITY OF THE HYDROGEN ATOMS OF THE METHYL GROUPS OF NITROTOLUENES

A.E. Porai-Koshits* and I.I. Chizhevskaya

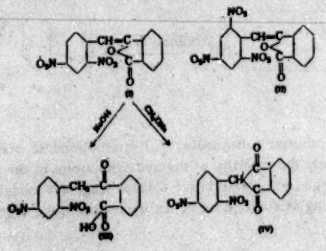
Investigations by one of us [1] have shown that the mobility of the hydrogen atoms of the methyl groups of various compounds may be evaluated on the basis of their ability to undergo condensation with aldehydes and nitroso compounds, as well as the azo-coupling reaction with diazo compounds; it was then established that condensation with aldehydes is the most general reaction, followed by condensation with nitroso compounds, and finally by the azo-coupling reaction. Compounds possessing an extremely high activity of the hydrogen atoms of the methyl groups undergo the last reaction.

Apart from the above-mentioned reactions, characteristic of compounds with labile hydrogen atoms of the methyl groups, it was shown in the case of quinaldine that these compounds are susceptible to condensation with phthalic anhydride (the phthalone reaction [2]). This reaction was successfully carried out by one of us in collaboration with A.I. Kulikov [3] in the case of biquinaldine, and a biquinophthalone derivative was obtained which was the product of condensation of 2 moles phthalic anhydride with 1 mole biquinaldine.

With the objective of further investigation of the ability of mobile hydrogen atoms of methyl groups to undergo condensation with phthalic anhydride, we have extended the phthalone reaction to nitro derivatives of toluene.

The mobility of the hydrogen atoms of the methyl groups of 2,4-dinitro- and 2,4,6-trinitrotoluenes has been demonstrated by their condensation with aldehydes [4] and nitroso compounds [5], as well as by azo-coupling (2,4,6-trinitrotoluene [6]). Mononitrotoluenes (ortho and para) are less reactive and do not react even with aldehydes.

Our experiments showed that 2,4-dinitro- and 2,4,6-trinitrotoluenes react with phthalic anhydride when the starting substances are heated in dimethylaniline. Mononitrotoluenes (ortho and para) remained indifferent to the action of phthalic anhydride. The properties of the products of condensation of 2,4-dinitro- and 2,4,6-trinitrotoluenes with phthalic anhydride, as well as the analytical data for the products, indicate that they are nitro derivatives of 3-(benzylidene)-phthalide, corresponding to Formulas (I) and (II).



*Deceased.

SOME PROPERTIES OF ENOL ACETATES

I. REACTION OF THE ENOL ACETATE OF CYCLOHEXANONE WITH N-BROMOSUCCINIMIDE

I. V. Machinskaya and V. A. Barkhash

In the present work we investigated the reaction of the enol acetate of cyclohexanone with N-bromosuccinimide with the aim of introducting the bromine atom into the allylic position of cyclohexenyl-Δ^1-acetate and of its later substitution.

A similar problem was previously attached by Djerassi and Scholz [1] who studied the reaction of the enol acetate of 3α-, 12α-diacetoxy-20-ketopregnane and of the 20-enol acetate of 3(β)-acetoxy-20-ketoallopregnane with N-bromosuccinimide. These chemists failed, however, to separate the corresponding bromo derivatives. They obtained unsaturated ketones whose formation may be accounted for by dehydrobromination of the initially formed bromo derivatives.

Similar results were obtained by Rubin and Armbrecht [2] who studied the reaction of the enol acetate of cholestanone-3 with N-bromosuccinimide. A report in the literature on the preparation of halo-substituted carbonyl compounds in a similar reaction relates to the case of application of N-iodosuccinimide [3].

By reaction of the enol acetate of cyclohexanone with N-bromosuccinimide we succeeded in obtaining the bromo derivative of this enol acetate which forms an addition compound with pyridine; on treatment with potassium iodide solution, this addition compound is transformed into the iodide, while with picric acid it gives a picrate of the composition $C_5H_5NC_8H_{11}O_2OC_6H_2(NO_2)_3$. Of these derivatives, only the picrate could be isolated in a pure form for analysis; the two other compounds were modified when attempts were made to purify them.

Bromination of the enol acetate might have been expected to lead to formation of 3-bromo-2-acetoxycyclohexene-1 or of 3-bromo-1-acetoxy-cyclohexene-1, or of a mixture of the two compounds. The fact that our bromo derivative distilled in a narrow range shows that in our case the reaction probably went predominantly in one of the directions indicated.

The prepared bromo derivative was reacted with sodium acetate and the resultant diacetoxy compound was hydrolyzed with the objective of determining the position of the bromine atom in the bromo derivative. Heating of bromo-cyclohexenyl acetate with anhydrous sodium acetate in glacial acetic acid gave a colorless crystalline product; m.p. 37-38.5°, distilling at 95-97° (5 mm). The data of elementary analysis correspond to the formula of diacetoxycyclohexene ($C_{10}H_{16}O_4$). Alkaline hydrolysis of diacetoxycyclohexene gave a colorless, crystalline substance, m.p. 114-115° and composition $C_6H_8O_2$. A mixture with the α-hydroxycyclohexanone obtained by hydrolysis of α-chlorocyclohexanone [4] did not give a depression of melting point.

Formation of α-hydroxycyclohexanone on hydrolysis of diacetoxycyclohexene shows that in the latter the acetoxy groups are at adjacent carbon atoms; consequently, in the reaction of cyclohexenyl-Δ^1-acetate with N-bromosuccinimide the bromine enters in the α-position to the carbon linked to the acetoxy group*. The 3-bromo-2-acetoxycyclohexene-1 and 2,3-diacetoxycyclohexene-1 obtained by us are not described in the literature.

We subsequently attempted to transform bromocyclohexenyl acetate into the corresponding acetoxycyclohexadiene.

*It is interesting to note that on bromination with N-bromosuccinimide of 1-chlorocyclohexene-1 another orientation of the introduced bromine (formation of 1-chloro-3-bromocyclohexene-1) is observed according to data of Mousseron, Winternitz and Jacquier [5].

The literature contains references to the employment of pyridine [6], sodium acetate [7], potassium acetate [8] and potassium carbonate [9] for the dehydrobromination of such compounds.

According to the data presented above, the reaction of 3-bromo-2-acetoxycyclohexene-1 with sodium acetate leads to formation of a diacetoxy derivative. Our attempt at dehydrobromination with the help of pyridine was likewise unsuccessful. On heating the product of addition of bromocyclohexenyl acetate to pyridine with 3 times the molar amount of pyridine for 3½ hours at the boiling point, we were unable to obtain any ether-soluble products. Evidently the product of addition decomposes under these conditions with evolution of hydrobromic acid.

EXPERIMENTAL

Preparation of cyclohexenyl-Δ^1-acetate. 100 g cyclohexanone was dissolved in 312 g acetic anhydride and to this was added 0.76 ml concentrated sulfuric acid; the mixture was set aside for 9 days at room temperature. To decompose the excess of acetic anhydride, the reaction mixture was treated with cold water with vigorous stirring and then solid soda was gradually added until it gave a slightly alkaline reaction. The reaction product was extracted with ether. The ethereal solution was washed with soda, then with water and was dried with sodium sulfate. The ether was driven off under the vacuum of a water-jet pump. The product had b.p. 52-55° at 4 mm. Yield 110 g (77%).

Reaction of enol acetate of cyclohexanone with N-bromosuccinimide. A mixture of 23.4 g N-bromosuccinimide, 20 g cyclohexenyl acetate (molar ratios 1:1) and 25 ml carbon tetrachloride was heated on a water bath in a flask fitted with reflux condenser. At bath temperature 72° a violent reaction began; the mixture at times had to be cooled with water. After the violent reaction ceased, all the bromosuccinimide went into solution. The succinimide which separated out upon cooling in the form of crystals was separated and its remains were removed by washing the reaction mixture with water. The organic layer was dried with sodium sulfate; carbon tetrachloride was driven off under the vacuum of an oil pump. The main bulk of the substance distilled at 81-82° (3 mm). Yield 18 g (57.6%). The product was unstable upon storage; it darkened and resinified.

Found %: Br 35.89, 35.49. $C_8H_{11}O_2Br$. Calculated %: Br 36.48.*

Addition product of bromocyclohexenyl acetate to pyridine may be prepared in the following manner. Equal quantities by weight of bromocyclohexenyl acetate and dry pyridine were mixed in a porcelain cup and left in a desiccator over sulfuric acid for 6 days. Pyridine was removed in a vacuum-desiccator in the course of several days. The obtained product, a sticky light-yellow mass, was dissolved in anhydrous alcohol and then to this solution was added absolute ether. The oil which separated out crystallized upon standing. The crystals were separated off, washed with absolute ether and then dried in a vacuum-desiccator, m.p. 113-130°.

Found %: Br 28.30. $C_{13}H_{16}O_2NBr$. Calculated %: Br 26.80.

Attempts to purify the product by recrystallization led to its decomposition.

Iodide $C_{13}H_{16}O_2NI$ was prepared by the action of a saturated solution of potassium iodide on a concentrated aqueous solution of the addition product of bromocyclohexenyl acetate to pyridine. Colorless crystals with m.p. 140-150°. An attempt to recrystallize the product from alcohol resulted in its decomposition.

Picrate $C_{19}H_{18}O_9N_4$ was prepared by the action of a saturated alcoholic solution of picric acid on an alcoholic solution of the addition product of bromocyclohexenyl acetate to pyridine. Yellow crystals with m.p. 143-144° (from alcohol).

Found %: N 12.43, 12.40. $C_{19}H_{18}O_9N_4$. Calculated %: N 12.55.

Reaction of bromocyclohexenyl acetate with sodium acetate. 20 g bromocyclohexenyl acetate, 18 g calcined sodium acetate and 35 g glacial acetic acid were heated in a flask fitted with reflux condenser on a water bath at the boiling point of the mixture for 2 hours. The reaction mixture, which crystallized upon cooling, was dissolved in a small quantity of water and neutralized with solid soda. The reaction product was repeatedly extracted with ether. The ethereal solution was washed with 15% soda solution, then with a small quantity of water and dried with sodium sulfate. The ether was driven off and the residue was transferred to a crystallizer. Upon standing, coarse crystals separated out which were separated from the oil and washed with a small quantity of

*The somewhat low bromine content as against the theoretical, evidently is due to partial decomposition of the product upon vacuum-distillation. The literature frequently notes [10] that upon heating, there takes place decomposition and evolution of hydrogen bromide in the case of bromo derivatives prepared by means of N-bromosuccinimide.

ether. Weight about 7 g; m.p. 34.5-38°, b.p. 95-97° (5 mm). Purification of the product by means of recrystallization was greatly hindered by the fact that in the cold it was readily soluble in alcohol, benzene and in carbon tetrachloride. Recrystallization from 50% ethyl alcohol did not yield a substance with a sharper melting point.

Assuming the presence in the prepared product of an admixture of the more water-soluble hydroxycyclohexane, which formed due to hydrolysis of the diacetoxy compound, we used the following method of purification. The reaction product was dissolved in a small quantity of alcohol, filtered and poured into water. After prolonged standing in an open vessel, large flaky crystals separated out with m.p. 37-39°.

Found %: C 60.60, 60.58; H 7.75, 7.66. $C_{10}H_{14}O_4$. Calculated %: C 60.59; H 7.12.

Alkaline hydrolysis of diacetoxycyclohexene. To a warm emulsion of diacetoxycyclohexene in 50% ethyl alcohol was added in the course of 20 minutes concentrated aqueous solution of caustic soda until the reaction was strongly alkaline. The reaction was accompanied by evolution of heat and the oil gradually went into solution. Upon cooling of the reaction mixture, a precipitate came down which was separated off and well washed with water. M.p. 75-82°. After 2 recrystallizations from alcohol, the product had m.p. 114-115°. A mixed sample with α-hydroxycyclohexanone gave no depression.

Found %: C 63.50; H 8.60. $C_6H_{10}O_2$. Calculated %: C 63.13; H 8.83.

SUMMARY

1. The procedure for preparation of the enol acetate of cyclohexanone was improved by interaction of cyclohexanone with acetic anhydride in presence of sulfuric acid; the yield of enol acetate reaches 77%.

2. 3-Bromo-2-acetoxycyclohexene-1, not previously described in the literature, was synthesized by reaction of the enol acetate of cyclohexanone with N-bromosuccinimide. The product of addition of 3-bromo-2-acetoxycyclohexene to pyridine was prepared, also the iodide and picrate of the addition compound.

3. It was established that heating of 3-bromo-2-acetoxycyclohexene-1 with sodium acetate in a medium of glacial acetic acid gives 2,3-diacetoxycyclohexene-1. The structure of the latter was confirmed by its transformation on alkaline hydrolysis onto α-hydroxycyclohexanone.

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REACTION OF β-CHLOROVINYL KETONES WITH β-DICARBONYL COMPOUNDS

II. THE KETOVINYLATION OF ALKYLMALONIC ESTERS

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Amont the diverse transformations of which β-chlorovinyl ketones are capable [1], a large group of reactions are known which resolve themselves into substitution of an atom of chlorine by some other grouping:

$$RCOCH = CHCl + HX \rightarrow RCOCH = CHX.$$

These reactions are essentially a general method of introduction of the ketovinyl radical into a molecule of an organic compound and we have therefore called them "ketovinylation reactions". Up to now details have been published of the ketovinylation of salts of some inorganic acids [2], alcohols [3], phenols [4], ammonia [5], amines [6], and phenolic ethers [7]. This reaction has been completely unknown, however, for compounds containing an active methylene or methine group. Panizzi [8] attempted to react phenyl-β-chlorovinyl ketone with malonic and acetoacetic esters but did not obtain a satisfactory result.

In the preceding communication [9] it was shown that β-chlorovinyl ketones react with acetoacetic ester in presence of potassium carbonate in boiling benzene with formation of alkylsalicylic acids, due to cyclization of the initial product of ketovinylation of acetoacetic ester. The rise in yield of salicylic acids with increasing excess of acetoacetic ester taken into the reaction and the separation of a secondary reaction product corresponding in composition to the product of transformation of bis-ketovinylated acetoacetic ester led us to the conclusion that β-chlorovinyl ketones react with compounds containing two mobile hydrogens with formation of a product of bis-ketovinylation. In this process the second molecule of β-chlorovinyl ketone reacts more easily than the first so that the remaining unsubstituted hydrogen atom of the methine group acquires greater mobility under the influence of the carbonyl group of the ketovinyl grouping in the molecule of the monoketovinylated derivative. Consequently, in the case of a compound containing only one mobile hydrogen atom, the reaction, if carried out under sufficiently mild conditions, must give the normal product of monoketovinylation.

With the objective of verifying this hypothesis and of developing new methods of organic synthesis on the basis of β-chlorovinyl ketones, we have studied the reactions of these compounds with alkylmalonic esters. Investigation showed that chlorovinyl ketones possessing a highly active halogen atom react with various alkylmalonic esters according to the general scheme:

$$RCOCH = CHCl + R'CH(COOC_2H_5)_2 \rightarrow RCOCH = CHC(R')(COOC_2H_5)_2$$

$R = CH_3$, C_2H_5, C_7H_{15}, C_6H_5; $R' = C_2H_5$, C_3H_7, C_4H_9.

The reaction was performed by gradual addition of the β-chlorovinyl ketone to the sodium compound of the alkylmalonic ester in benzene; the reaction is energetic even in the cold, and heating is necessary only to complete it. After the usual working-up, the product is separated by vacuum distillation. Performance of the reaction by the classical procedure of the malonic synthesis in excess of alcohol appears very inexpedient because β-chlorovinyl ketones react with very great facility with alcohols with formation of β-ketoacetals [3].

The reaction is general in character, and we investigated it with reference to methyl-, ethyl-, heptyl- and phenyl-β-chlorovinyl ketones. Of the malonic esters we selected ethyl-, propyl- and butylmalonic esters.

The alkyl-β-chlorovinyl ketones required for the research were prepared by the method previously developed in our laboratory [10]. One of them – heptyl-β-chlorovinyl ketone – obtained by a similar method, is described for the first time.

The products of reaction, obtained in fairly high yields, are oily liquids which distill in vacuum without decomposition (10 mm) and are stable when kept. The analyses and constants of the products indicate that they are products of normal ketovinylation and have the structure of the corresponding alkyl-(γ-ketoalkenyl)-malonic esters. As we know [11], β-chlorovinyl ketones react with organomagnesium compounds and with sodium compounds of acetylenic hydrocarbons at their carbonyl group, the β-chlorovinyl radical remaining intact. In our case, however, the reaction follows the usual route of the malonic synthesis and is expressed by the scheme presented above. The proposed structure of the prepared compounds is supported by the retention in them of the carbonyl group, as confirmed by the formation of dinitrophenylhydrazones and by the presence of an intact double bond, as shown by catalytic hydrogenation of one of the prepared substances over palladium on barium sulfate:

$$CH_3COCH{=}CHC(COOC_2H_5)_2 \xrightarrow[Pd/BaSO_4]{H} CH_3COCH_2CH_2C(COOC_2H_5)_2$$
$$\quad\quad\quad

After a second distillation, the substance had the following constants: b.p. 163-164° (12 mm), 156-157° (10 mm), 125-126° (2 mm), 118-119° (0.5 mm), d_4^{20} 1.0598, n_D^{20} 1.4543, MR_D 65.52; calc. 65.08. Yield 28.5 g (55.6%).

Found %: C 61.33, 61.41; H 7.95, 8.08. $C_{13}H_{20}O_5$. Calculated %: C 60.92; H 7.86.

Ethyl-(3-ketobutenyl-1)-malonic ester was a colorless oil, miscible with organic solvents and insoluble in water.

Dinitrophenylhydrazone. To solid 2,4-dinitrophenylhydrazine was added several drops of substance, 2 drops of methanol, 1 drop concentrated hydrochloric acid, the mass was heated for 3 minutes on a steam bath and the hydrazone which formed melted and then solidified upon cooling and shaking. After recrystallization from alcohol, orange crystals with m.p. 108°.

Found %: N 13.05, 13.03. $C_{19}H_{24}O_9N_4$. Calculated %: N 12.84.

All the other products of ketovinylation of alkylmalonic esters were prepared under the same conditions, only the quantity of absolute benzene was changed and was taken proportionally to the components taken for reaction. Dinitrophenylhydrazones of other alkyl-(γ-ketoalkenyl)-malonic esters were prepared according to the above-presented prescription.

3. Propyl-(3-ketobutenyl)-malonic ester. Propyl-(3-ketobutenyl-1)-malonic ester was prepared from 5.8 g sodium, 53 g propylmalonic ester and 26.2 g methyl-β-chlorovinyl ketone in 375 ml absolute benzene. Upon vacuum-distillation, the fraction was collected with b.p. 160-165° (8 mm), yield 38 g (56.3%).

After a second distillation, the substance had the following constants: b.p. 163° (8 mm), d_4^{20} 1.0437, n_D^{20} 1.4553, MR_D 70.31; calc. 69.70.

Found %: C 62.88, 62.61; H 8.49, 8.41. $C_{14}H_{22}O_5$. Calculated %: C 62.20; H 8.20.

Dinitrophenylhydrazone – orange crystals with m.p. 119° (from alcohol).

Found %: N 12.43, 12.27. $C_{20}H_{26}O_9N_4$. Calculated %: N 12.44.

4. Butyl-(3-ketobutenyl-1)-malonic ester. Butyl-(3-ketobutenyl-1)-malonic ester was prepared from 5.8 g sodium, 56.7 g butylmalonic ester and 26.2 g methyl-β-chlorovinyl ketone in 375 ml absolute benzene. Upon vacuum-distillation, the fraction was collected with b.p. 160-164° (6 mm), yield 25.0 g (35.2%).

After a second distillation, the substance had the following constants: b.p. 154-156° (4 mm), d_4^{20} 1.0326, n_D^{20} 1.4559, MR_D 74.84; calc. 74.32.

Found %: C 63.07, 63.10; H 8.59, 8.58. $C_{15}H_{24}O_5$. Calculated %: C 63.35; H 8.51.

The semicarbazone was prepared by the usual method. Colorless crystals with m.p. 90° (from alcohol).

Found %: N 12.09, 12.77. $C_{16}H_{27}O_5N_3$. Calculated %: N 12.31.

5. Propyl-(3-ketopenten-1-yl-1)-malonic ester. Propyl-(3-ketopenten-1-yl-1)-malonic ester was prepared from 6 g sodium, 54.5 g propylmalonic ester and 30.8 g ethyl-β-chlorovinyl ketone in 380 ml absolute benzene. Upon distillation, the fraction was collected with b.p. 168-175° (9 mm), yield 44.0 g (94%).

After a second distillation, the substance had the following constants: b.p. 169-171° (9 mm), d_4^{20} 1.0350, n_D^{20} 1.4575, MR_D 74.89; calc. 74.32.

Found %: C 63.27, 63.35; H 8.64, 8.62. $C_{15}H_{24}O_5$. Calculated %: C 63.35; H 8.51.

Dinitrophenylhydrazone – orange crystals with m.p. 124° (from alcohol).

Found %: N 12.64, 12.64. $C_{21}H_{28}O_9N_4$. Calculated %: N 12.06.

6. Propyl-(3-ketodecen-1-yl-1)-malonic ester. Propyl-(3-ketodecen-1-yl-1)-malonic ester was prepared from 5.1 g sodium, 49 g propylmalonic ester and 42 g heptyl-β-chlorovinyl ketone in 330 ml absolute benzene. Upon distillation, the fraction was collected with b.p. 177-185° (1 mm), yield 54.5 g (70%).

After a second distillation, the substance had the following constants: b.p. 177-178° (1 mm), d_4^{20} 0.9901, n_D^{20} 1.4581, MR_D 97.71; calc. 97.41.

Found %: C 67.19, 67.09; H 9.82, 9.95. $C_{20}H_{34}O_5$. Calculated %: C 67.76; H 9.66.

7. Propyl-(3-phenylpropen-1-on-3-yl-1)-malonic ester was prepared from 4 g sodium, 36.4 g propylmalonic ester and 28 g phenyl-β-chlorovinyl ketone [12] in 260 ml absolute benzene. Upon distillation, the fraction was collected with b.p. 206-208° (4 mm), yield 36 g (63.7%).

After distillation, the substance had the following constants: b.p. 204-205° (4 mm), d_4^{20} 1.1007, n_D^{20} 1.5112, MR_D 90.50; calc. 89.19. After prolonged standing, the substance completely crystallized. Recrystallization from alcohol yielded colorless needles with m.p. 39°.

Found %: C 68.84, 68.84; H 7.51, 7.41. $C_{19}H_{24}O_5$. Calculated %: C 68.65; H 7.26.

Dinitrophenylhydrazone – orange needles with m.p. 183-184° (from alcohol).

Found %: N 11.05, 11.09. $C_{25}H_{28}O_9N_4$. Calculated %: N 10.94.

8. Hydrogenation of ethyl-(3-ketobutenyl)-malonic ester. 14.0 g ethyl-(3-ketobutenyl)-malonic ester was hydrogenated in 100 ml alcohol over palladium precipitated on barium carbonate. After absorption of 1206 ml hydrogen (0°, 760 mm), hydrogenation ceased. The calculated amount was 1300 ml hydrogen. The catalyst was filtered off and after driving off the alcohol, the residue was vacuum distilled. Yield of ethyl-(3-ketobutyl)-malonic ester 12.2 g (83%).

After a second distillation, the substance had the following constants: b.p. 133-134° (2 mm), d_4^{20} 1.0499, n_D^{20} 1.4436, MR_D 65.36; calc. 65.55.

Found %: C 60.22, 60.31; H 8.60, 9.07. $C_{13}H_{22}O_5$. Calculated %: C 60.44; H 8.59.

The product was a colorless oil, stable on standing and miscible with organic solvents and insoluble in water.

9. Saponification of ethyl-(3-ketobutyl)-malonic ester. 10 g ethyl-(3-ketobutyl)-malonic ester was boiled for 1.5 hours with a solution of 9 g caustic potash in 90 ml 88% alcohol and, on cooling, the mixture was poured in 700 ml water, extracted with ether; the aqueous layer was acidified; the oil which came down was extracted with ether. The ethereal extract was extracted with 5% caustic soda solution, the alkaline solution was acidified, the oil which came down was extracted with ether, the extract was dried over sodium sulfate, the ether was driven off, the oily residue after drying in vacuum desiccator for several days completely crystallized. Yield 3.7 g (47.4%). After recrystallization from a mixture of benzene and petroleum ether, ethyl-(3-ketobutyl)-malonic acid was in the form of colorless crystals with m.p. 106°.

Found %: C 53.74, 53.81; H 7.15, 7.07. $C_9H_{14}O_5$. Calculated %: C 53.46; H 6.98.

SUMMARY

1. A study is made of the reactions of β-chlorovinyl ketones with alkylmalonic esters which lead to formation of alkyl-(γ-ketoalkenyl)-malonic esters, thus providing a method of synthesis for compounds of this type.

2. The structure of the compounds prepared is confirmed by preparation of the dinitrophenylhydrazones and by catalytic hydrogenation.

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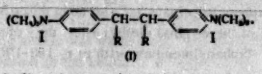
*T.p. = C.B. Translation pagination.

NITROGEN-CONTAINING DERIVATIVES OF ESTERS OF MESO-α,α'-DIPHENYLSUCCINIC ACID

S.F. Torf and N.V. Khromov-Borisov

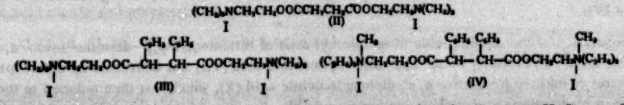
It was earlier observed [1] that among derivatives of diphenylethane with the general Formula (I), where R = H or alkyl, are compounds possessing prolonged curare-like activity. In the same work it was shown that the meso form of Compound (I) when R = C_6H_5 has a considerably higher curare-like activity than the racemate:



(I)

Continuing our investigations in this direction, we decided to introduce carbethoxy groups as radicals R in Compound (I) in order to establish whether this change would influence the curare-like activity. With this objective we synthesized the diethyl ester of meso-α,α'-diphenylsuccinic acid containing two quaternary ammonium groups at the benzene rings (I, R = $COOC_2H_5$).

On the other hand we know that the iodide of the dicholine ester of succinic acid (ditilin) (II) possesses a considerable short-period curare-like activity [2,3,4]. It appeared of interest to synthesize the dicholine ester of meso-α,α'-diphenylsuccinic acid (III) whose structure is that of a diphenylated derivative of ditilin. In order to clarify the effect of substitution in Compound (III) of methyl radicals by ethyls, Compound (IV) was synthesized which is likewise a derivative of meso-α,α'-diphenylsuccinic acid:

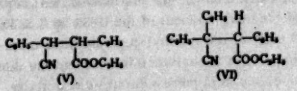


(III) (IV)

α,α'-Diphenylsuccinic acid was obtained by the method described in the literature [5-8]: α-phenylcinnamonitrile → α,α'-diphenylsuccinonitrile → α,α'-diphenylsuccinic acid. This method gave a mixture of meso (73.1%) and racemic (19.7%) α,α'-diphenylsuccinic acids; the acids were transformed into the barium salts for the purpose of resolution.

α-Cyano-α'-carbethoxy-α,α'-diphenylethane (V) was prepared by a new method from benzyl cyanide and ethyl α-bromophenylacetate with the help of sodium ethoxide. Compound (V) was then saponified to meso-α,α'-diphenyl-succinic acid. α-Cyano-α'-carbethoxy-α,α'-diphenylethane contains two asymmetric carbon atoms and is therefore obtained in the form of two racemates. Thus it was possible to isolate only one of the racemates, from which after saponification only meso-α,α'-di-phenylsuccinic acid was obtained.

By an anlogous sequence of reactions, α-cyano-α'-carbethoxy-α,α,α'-triphenylethane (VI) was prepared from diphenylacetonitrile and ethyl α-bromophenylacetate with the help of sodium ethoxide. Compound (VI) is a derivative of triphenylsuccinic acid.

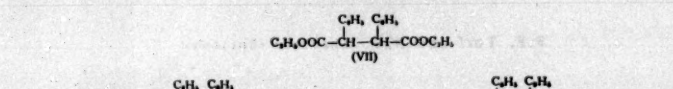


(V) (VI)

Ethyl α-bromophenylacetate was synthesized by a modification of the method of Tiffeneau and Fourneau [9] whereby phenylacetyl chloride [10] was not separated. Diphenylacetonitrile was obtained by the literature method [11].

We synthesized the above-mentioned compounds (I, R = $COOC_2H_5$, III and IV) in the following manner: from meso-α, α'-diphenylsuccinic acid we prepared the dichloride, previously synthesized by McRae and Townshend with the help of phosphorus pentachloride [12] but without indication of yield. We found that the formation of this dichloride goes very much better if the reaction with phosphorus pentachloride is conducted with addition of phosphorus oxychloride since a homogeneous solution is then formed during the reaction. Yield 75.1%.

Reaction of the dichloride of meso-α, α'-diphenylsuccinic acid with ethyl alcohol, dimethylaminoethanol and diethylaminoethanol gave the corresponding esters (VII, VIII, IX).

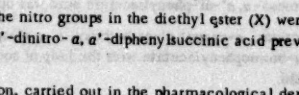


Preparation of diethyl meso-α, α'-diphenylsuccinate by this method has been described previously [12]. Bis-(β-diethylaminoethyl)-α, α'-diphenylsuccinate has also been described [13]. As the authors point out, regardless of the stereoisomeric form of the original diethyl ester, they obtained one and the same dihydrochloride of bis-(β-diethylaminoethyl)-α, α'-diphenylsuccinate with m.p. 188-190°.

It is known [14] that heating in alcoholic solution in presence of sodium ethoxide leads to transformation of both the meso form and of the racemate of diethyl α, α'-diphenylsuccinate into an equilibrium mixture of the stereoisomeric forms. But since the above authors carried out transesterification in presence of sodium diethylaminoethylate, they were bound to have obtained an equilibrium mixture of the meso form and the racemate of the diethylaminoethyl ester of α, α'-diphenylsuccinic acid; hence the dihydrochloride obtained from this mixture could have the same melting point in both cases (188-190°).

The bis-(β-diethylaminoethyl)meso-α, α'-diphenylsuccinate that we synthesized had m.p. 58-60°, and its dihydrochloride had m.p. 205-207°. Reaction of the bis-(β-dimethylaminoethyl) and bis-(β-diethylaminoethyl) esters of meso-α, α'-diphenylsuccinic acid with methyl iodide led to the corresponding bis-ammonium derivatives (III and IV).

For preparation of the dimethiodide of the diethyl ester of tetramethyl-p,p'-diamino-meso-α, α'-diphenylsuccinic acid, the diethyl ester of meso-α, α'-diphenylsuccinic acid (VII) was converted by direct nitration into the diethyl ester of meso-p,p'-dinitro-α, α'-diphenylsuccinic acid (X), which was then reduced to the diethyl ester of meso-p,p'-diamino-α, α'-diphenylsuccinic acid (XI). Reaction of the latter with methyl iodide in presence of calcium carbonate in dilute ethyl alcohol gave the dimethiodide of the diethyl ester of tetramethyl-p,p'-diamino-meso-α, α'-diphenylsuccinic acid (I, R = $COOC_2H_5$).



The p- and p'-positions of the nitro groups in the diethyl ester (X) were confirmed by synthesis of the same ester by esterification of meso-p,p'-dinitro-α, α'-diphenylsuccinic acid previously described in the literature [8, 12].

Pharmacological investigation, carried out in the pharmacological department of the Institute of Experimental Medicine of the Academy of Medical Sciences of the USSR by S.S. Krylov and A.I. Podlesnaya, showed that the dimethiodide of the diethyl ester of tetramethyl-p,p'-diamino-meso-α, α'-diphenylsuccinic acid, the iodide of the dicholine ester of meso-α, α'-diphenylsuccinic acid and the dimethiodide of bis-(β-diethylaminoethyl) ester of meso-α, α'-diphenylsuccinic acid possess curare-like activity.

EXPERIMENTAL

α-Cyano-α'-carbethoxy-α, α'-diphenylethane (V). To a solution of 23.4 g benzyl cyanide and 48.6 g ethyl ester of α-bromophenylacetic acid, containing no hydrogen bromine (test on Congo), with stirring and cooling in a freezing mixture was added in the course of 20 minutes a solution of sodium alcoholate (4.9 g sodium in 120 ml anhydrous alcohol); to wash off the residual solution of sodium alcoholate, 30 ml more anhydrous alcohol was added. Towards completion of adding the alcoholate solution, the contents of the reaction flask thickened. Stirring was continued for 45 minutes more. On the next day, the precipitate was filtered off and washed 4-5 times with alcohol from the colored mother liquor. The precipitate was then mixed in 200 ml water, filtered off, washed with water and dried at 50°. Weight 25 g. After recrystallization from 400 ml alcohol in the presence of activated charcoal, 21 g (37.6%) of Substance (V) was obtained with m.p. 139-140°. Alcohol was driven off from the basic alcoholic mother liquor, the residue was treated with water and extracted with ether, dried with calcium chloride and after driving off the ether, the residue was vacuum-distilled. At 76-102° (1-2 mm) we obtained 15.4 g of a quite mobile fraction with a pleasant ester odor, not investigated further. At 165-178° (1-2 mm) we obtained 2.8 g of viscous oil. Due to incipient decomposition, distillation was halted. After recrystallization of 2.8 g of the fraction from 10 ml alcohol, we obtained 0.5 g α-cyano-α'-carbethoxy-α, α'-diphenylethane with m.p. 136-137°.

Found %: C 77.33, 77.58; H 6.19, 6.18; N 5.03, 4.99. $C_{18}H_{17}O_2N$. Calculated %: C 77.42; H 6.09; N 5.02.

α-Cyano-α'-carbethoxy-α, α, α'-triphenylethane (VI). To a warm solution of sodium alcoholate (2.4 g sodium in 65 ml anhydrous alcohol) was added with stirring 19.3 g fused diphenylacetic acid nitrile and 15 ml anhydrous alcohol with which the remaining nitrile was washed off. The resulting hot solution was cooled in a freezing mixture and to the resulting suspension in the course of 20 minutes was added 24.3 g ethyl ester of α-bromophenylacetic acid and then 20 ml anhydrous alcohol with which the remaining ester was washed off and the temperature of the reaction mixture rose to 14°. After 30 minutes, the dense friable precipitate that adhered to the walls was broken up slightly and then the whole mass was stirred again for 1 hour with cooling. The heterogeneous light-lemon coloration of the precipitate went to a homogeneous white. On the next day, the precipitate was filtered off, washed with alcohol, mixed with 200 ml water and filtered off. The weight of the air-dried substance was 27.8 g. After recrystallization from 600 ml alcohol, we obtained 21.7 g α-cyano-α'-carbethoxy-α, α, α'-triphenylethane with m.p. 165-166°. After driving off the main bulk of the alcohol, we isolated 2 g more of pure substance with m.p. 164-165°. Total yield was 66.8%.

The same yield of product was obtained when the solution of sodium alcoholate was added to a mixture of diphenylacetic acid nitrile and ethyl ester of α-bromophenylacetic acid.

Found %: C 81.10, 81.26; H 5.88, 5.97; N 4.02, 4.08. $C_{24}H_{21}O_2N$. Calculated %: C 81.13; H 5.91; N 3.94.

α, α'-Diphenylsuccinic acid. a) 75 g dinitrile of α, α'-diphenylsuccinic acid (m.p. 205°) was hydrolyzed by the Wawzonek method [7]. The reaction mixture was diluted with water and converted to a solution by addition of a solution of 30.5 g caustic soda in 375 ml water [15]. To the neutralized filtered solution of the sodium salt was added a solution of 25 g barium chloride in 200 ml water. The precipitate which came down of the barium salt of the racemate of α, α'-diphenylsuccinic acid was filtered off. The filtrate, containing the barium salt of meso-α, α'-diphenylsuccinic acid, was heated to 70° and to it was added 90 ml concentrated hydrochloric acid, diluted with 100 ml water. The precipitate which came down was filtered off while hot, washed with hot water and dried at 100°. The weight of meso-α, α'-diphenylsuccinic acid was 63.5 g (73.1%), m.p. 227-229°.

In order to isolate the racemate of α, α'-diphenylsuccinic acid, its barium salt was boiled for 2 hours with 500 ml water and 12 ml concentrated sulfuric acid. The insoluble precipitate was filtered off while hot and washed with hot water. After cooling, the precipitate of the racemate was filtered off. The weight of the air-dried precipitate was 7 g, m.p. 183-185°. The insoluble precipitate was again boiled with the filtrate and wash waters (850 ml). The precipitate of $BaSO_4$ was filtered off while hot. After cooling, from the filtrate was isolated 11.3 g more racemate with m.p. 183-185°. Yield of racemate of α, α'-diphenylsuccinic acid, containing 1 molecule water [8], 19.7%.

b) A mixture of 27.2 g α-cyano-α'-carbethoxy-α, α'-diphenylethane (V), 68 ml water, 68 ml concentrated sulfuric acid and 34 ml acetic acid was boiled under reflux for 7 hours; the ester at first melted and then a solid precipitate began to form.

About 10 ml liquid was driven off from the reaction flask, from which about 6 ml ethyl acetate separated out after dilution with water. About 5 ml more acetic acid was added to the reaction flask, the mixture was boiled for 6 hours more, was diluted with water and after cooling, the precipitate was filtered off and was converted to a solution as the sodium salt, as described in Method "a".

The solution which did not contain the racemate of *a, a'*-diphenylsuccinic acid (test with $BaCl_2$ gave a negative result), was acidified with hydrochloric acid. The precipitate which came down was filtered off while hot and dried at 100°. The weight of meso-*a, a'*-diphenylsuccinic acid was 24.3 g (92.3%), m.p. 227-229°.

Found %: C 70.81, 70.77; H 5.26, 5.19. $C_{16}H_{14}O_4$. Calculated %: C 71.10; H 5.20.

A mixed sample of meso-*a, a'*-diphenylsuccinic acid, prepared by two different methods, had m.p. 227-229°.

Meso-*a, a'*-diphenylsuccinyl dichloride. 37.8 g meso-*a, a'*-diphenylsuccinic acid was mixed with 59.5 g phosphorus pentachloride. To the mixture was added 40 ml phosphorus oxychloride and the reaction flask was fitted with a reflux condenser with calcium chloride tube. Upon shaking manually for a short time, a smooth reaction began with evolution of hydrogen chloride. Heating was carried out on a water bath for about 45 minutes and finally at 100° until solution of meso-*a, a'*-diphenylsuccinic acid; solution of the latter served to indicate the end of the reaction. Phosphorus oxychloride (52 ml) was driven off on a water bath (50-60°, 40-50 mm). The residue was recrystallized from 175 ml benzene, washed with benzene until the yellow color disappeared and dried in air. The weight of meso-*a, a'*-diphenylsuccinyl dichloride was 32.3 g (75.1%), m.p. 186-188°. The dichloride was soluble in the cold in chloroform.

Diethyl ester of meso-*a, a'*-diphenylsuccinic acid. A mixture of 7.2 g meso-*a, a'*-diphenylsuccinyl chloride and 90 ml anhydrous alcohol was boiled with a reflux fitted with calcium chloride tube for several hours on a water bath. Upon cooling, crystals began to come down from the warm solution. After cooling, the precipitate was filtered off, washed with alcohol and dried at 60°. The weight of diethyl ester of meso-*a, a'*-diphenylsuccinic acid was 7 g (91.6%), m.p. 140-141°.

Bis-(β-dimethylaminoethyl) ester of meso-*a, a'*-diphenylsuccinic acid. To 9 ml dimethylaminoethanol was added in the course of 5 minutes 3 g meso-*a, a'*-diphenylsuccinic acid upon cooling in a water bath. Heating was carried out on an oil bath (110-120°) with air condenser, fitted with calcium chloride tube, for 1.5 hours until solution of the precipitate. The excess of dimethylaminoethanol was driven off in vacuum at 100°. To the residue, after cooling, was added 20 ml water and the whole mass was heated to 50°. The softened precipitate was stirred for a short time in water and, after cooling, was filtered off and dried at 60°. During drying, the precipitate softened. The dried precipitate (3.7 g) was dissolved in 25 ml acetone and upon cooling with water, through the filtered solution was passed hydrogen chloride for several minutes until the solution gave an acid reaction (on Congo). Cooling was carried out overnight with ice. The precipitate was filtered off and dried in air. Weight 1.9 g, m.p. 232-233.5°. The precipitate was dissolved with heating in a mixture of 4 ml water and 20 ml acetone and to the hot solution was added 20 ml more of acetone. After cooling, the precipitate which came down was filtered off, washed with acetone and dried in air. Yield 1.6 g (34%) meso-*a, a'*-diphenylsuccinic acid bis-(β-dimethylaminoethyl) ester dihydrochloride, m.p. 239-240°.

Found %: C 59.38, 59.46; H 7.00, 7.11; N 5.45, 5.28; Cl 14.25, 14.27. $C_{24}H_{34}O_4N_2Cl_2$. Calculated %: C 59.38; H 7.01; N 5.78; Cl 14.64.

Upon analysis for chlorine (gravimetrically), it proved necessary to wash the precipitate of AgCl several times with warm dilute nitric acid, since the nitrite of the base precipitated together with AgCl due to its sparing solubility in water.

The free base was isolated by running a solution of 0.4 g dihydrochloride in 10 ml water into a filtered solution of 0.5 g potash in 10 ml water. After an hour, the precipitate which came down was filtered off, washed with water and dried in a vacuum desiccator. Yield 0.33 g bis-(β-dimethylaminoethyl) ester of meso-*a, a'*-diphenylsuccinic acid, m.p. 93-95°. Quantitative yield.

Found %: N 6.74, 6.53. $C_{24}H_{32}O_4N_2$. Calculated %: N 6.80.

Bis-(β-diethylaminoethyl) ester of meso-*a, a'*-diphenylsuccinic acid. 20 g meso-*a, a'*-diphenylsuccinyl dichloride was added in the course of 1 hour with water-cooling to 60 ml diethylaminoethanol and then heating was conducted with an air condenser fitted with a calcium chloride tube until solution of the precipitate (2.5 hours at 120-130° on an oil bath). The excess of diethylaminoethanol was driven off in vacuum on a water bath.

After cooling, water was added to the residue. The oily residue, the main bulk of which solidified after 30 minutes, was filtered off, washed with water and dried in vacuum on a boiling water bath. It was dissolved in 110 ml acetone and upon being cooled in a freezing mixture, hydrogen chloride was passed into the solution until it gave an acid reaction (on Congo). After 2 hours, the precipitate was filtered off, washed with acetone and purified by solution with heating in dilute acetone (20 ml water and 120 ml acetone) and by boiling with activated charcoal. The hot filtrate was diluted with 300 ml acetone. After being cooled in a freezing mixture for 2 hours, the precipitate was filtered off, washed with acetone and dried in air. The weight of meso-*a*, *a*'-diphenylsuccinic acid bis-(β-diethylaminoethyl) ester dihydrochloride was 12 g (34%), m.p. 205-206°.

Found %: C 61.83, 62.00; H 7.89, 7.79; N 5.38, 5.35; Cl 12.94, 12.93. $C_{28}H_{42}O_4N_2Cl_2$. Calculated %: C 62.11; H 7.76; N 5.37; Cl 13.13.

The free base was isolated from the aqueous solution of the dihydrochloride by neutralization with aqueous potash solution as in the preceding experiment. The suspension which formed soon converted to a crystalline precipitate which was filtered off, washed with water and dried in a vacuum desiccator. The bis-(β-diethylaminoethyl) ester of meso-*a*, *a*'-diphenylsuccinic acid had m.p. 58-60°. Quantitative yield.

Found %: N 5.95, 6.19. $C_{28}H_{40}O_4N_2$. Calculated %: N 5.98.

Iodide of dicholine ester of meso-*a*, *a*'-diphenylsuccinic acid (III). 1.25 g bis-(β-dimethylaminoethyl) ester of meso-*a*, *a*'-diphenylsuccinic acid was dissolved in 25 ml acetone and to the solution with shaking was added 1 ml methyl iodide. A white precipitate immediately came down, which on the next day was filtered off and washed with acetone. Weight 1.95 g. The precipitate was recrystallized from 20 ml water and washed with water and acetone. Yield 1.55 g (73.5%) iodide of dicholine ester with m.p. 251-253°.

Found %: N 3.92, 4.02; I 36.10, 36.14. $C_{26}H_{38}O_4N_2I_2$. Calculated %: N 4.03; I 36.40.

Dimethiodide of bis-(β-diethylaminoethyl) ester of meso-*a*, *a*'-diphenylsuccinic acid (IV). To a solution of 1.7 g bis-(β-diethylaminoethyl) ester of meso-*a*, *a*'-diphenylsuccinic acid in 30 ml acetone was added 1 ml methyl iodide with shaking. The white precipitate which came down after several minutes was filtered off the next day. Weight 2.7 g. After recrystallization from 15 ml water, washing the precipitate with water and acetone, we obtained 2 g (73.3%) dimethiodide with m.p. 225-226°.

Found %: N 3.60, 3.65; I 33.56, 33.49. $C_{30}H_{46}O_4N_2I_2$. Calculated %: N 3.72; I 33.77.

Meso-p,p'-dinitro-*a*, *a*'-diphenylsuccinic acid. To 50 ml nitric acid (d 1.52), cooled in a freezing mixture, was added in the course of one hour with stirring 10 g meso-*a*, *a*'-diphenylsuccinic acid. The temperature rose from -4 to +2°. After stirring and cooling was continued for 30 minutes more, the whole mass was poured on ice. The precipitate was filtered off, washed with water and dried at 60°. The dried precipitate (12.8 g) was boiled for 1 hour with 200 ml acetic acid. The insoluble precipitate was filtered off while hot and washed with acetic acid. The weight of the dried precipitate was 8.5 g, m.p. 227-228°. This precipitate was dissolved in 60 ml water with 5 ml concentrated ammonia solution; the solution was boiled with activated charcoal and the hot filtrate was poured in 100 ml hot acetic acid, containing 10 ml concentrated acid. The precipitate which came down was filtered off while hot, washed with hot acetic acid, with water and dried at 100°. Yield 7.5 g (56.4%) meso-p,p'-dinitro-*a*, *a*'-diphenylsuccinic acid with m.p. 238-240°.

Diethyl ester of meso-p,p'-dinitro-*a*, *a*'-diphenylsuccinic acid (X). a) 1 g meso-p,p'-dinitro-*a*, *a*'-diphenylsuccinic acid was boiled with a reflux condenser fitted with calcium chloride tube for 27 hours with 30 ml anhydrous alcohol and 1 ml concentrated sulfuric acid and was filtered while hot from the slight admixture. After cooling, the precipitate which came down was filtered off. The weight of dry precipitate was 0.65 g, m.p. 152-159°. The precipitate was treated with potash solution, filtered off, washed with water, dried and recrystallized from 25 ml alcohol. Yield 0.45 g (38.8%) white diethyl ester of meso-p,p'-dinitro-*a*, *a*'-diphenylsuccinic acid with m.p. 159-161°.

b) 2.5 g diethyl ester of meso-*a*, *a*'-diphenylsuccinic acid was added in the course of 10 minutes to 10 ml nitric acid (d 1.51) with stirring and cooling in a freezing mixture. The temperature rose from -5 to +2°. Then, upon cooling, the whole mass was stirred for 10 minutes more and poured on ice. The precipitate was filtered off, dried at 50° (3.1 g) and recrystallized from 70 ml alcohol. Yield 2 g (62.7%) white diethyl ester of meso-p,p'-dinitro-*a*, *a*'-diphenylsuccinic acid with m.p. 159-161°. A mixed sample, prepared by Method "a", gave no melting point depression.

Found %: C 57.96, 57.69; H 4.91, 4.92; N 6.70, 6.74. $C_{20}H_{20}O_8N_2$. Calculated %: C 57.69; H 4.81; N 6.73.

Diethyl ester of meso-p,p'-diamino-α,α'-diphenylsuccinic acid (XI). A mixture of 2 g diethyl ester of meso-p,p'-dinitro-α,α'-diphenylsuccinic acid, 4.5 g calcium carbonate, 8.5 g stannous chloride ($SnCl_2 \cdot 2H_2O$) and 40 ml alcohol was boiled on a water bath with reflux condenser for 5 hours. The slurrylike mass which formed was stirred well once with a rod during heating. After cooling, the mixture was diluted with 160 ml water, the precipitate was filtered off, washed with a small quantity of water (there was noted a retardation in the rate of filtering) and dried at 60°. The dry precipitate was boiled with 40 ml benzene and the pale-yellow solution was filtered off while hot from the precipitate through a glass filter. A precipitate started to come down from the still warm filtrate. After cooling, the precipitate was filtered off and washed with benzene. The weight of the air-dried diethyl ester of meso-p,p'-diamino-α,α'-diphenylsuccinic acid was 0.9 g with m.p. 186-187°. After dilution of the benzene mother liquor with the same volume of petroleum ether, we isolated 0.3 g (70.2%) more of the ester, which had a cream-colored tinge. M.p. 183-185°.

When the reduction was carried out without addition of calcium carbonate, the reaction went faster but the reaction product, isolated by pouring the cooled reaction solution into an aqueous solution of potash and recrystallized from benzene, melted several degrees below the cited melting point.

Found %: C 67.40, 67.48; H 6.79, 6.86; N 7.95, 7.85. $C_{20}H_{24}O_4N_2$. Calculated %: C 67.41; H 6.74; N 7.85.

Dimethiodide of diethyl ester of tetramethyl-p,p'-diamino-meso-α,α'-diphenylsuccinic acid (I, R=$COOC_2H_5$). A mixture of 0.9 g diethyl ester of meso-p,p'-diamino-α,α'-diphenylsuccinic acid, 0.6 g calcium carbonate, 10 ml ethyl alcohol, 5 ml water and 1.8 ml methyl iodide was boiled under reflux on a water bath for 5 hours. After cooling in a freezing mixture, the precipitate was filtered off and recrystallized with activated charcoal from 10 ml water. Yield 0.75 g (42.6%) of dimethiodide of the diethyl ester of tetramethyl-p,p'-diamino-meso-α,α'-diphenylsuccinic acid with m.p. 212-214°.

Found %: N 4.13, 3.97; I 36.38, 36.59. $C_{36}H_{58}O_4N_2I_2$. Calculated %: N 4.02; I 36.54.

SUMMARY

1. The following derivatives of meso-α,α'-diphenylsuccinic acid, containing two quaternary ammonium groups were synthesized: the iodide of the dicholine ester of meso-α,α'-diphenylsuccinic acid, the dimethiodide of the bis-(β-diethylaminoethyl) ester of meso-α,α'-diphenylsuccinic acid, and the dimethiodide of the diethyl ester of tetramethyl-p,p'-diamino-meso-α,α'-diphenylsuccinic acid.

2. Meso-α,α'-diphenylsuccinic acid was obtained by a new method: from benzyl cyanide and the ethyl ester of α-bromophenylacetic acid in presence of sodium ethoxide.

3. All three esters possess curare-like activity.

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DERIVATIVES OF PYRIDO-(3,2-d)-THIAZOLE

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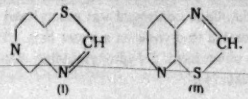
The synthesis of pyrido-(3,4-d)-thiazole (I) and of some of its derivatives was described in the previous communication [1].

It appeared of interest to obtain analogous derivatives of pyrido-(3,2-d)-thiazole (II) and to compare their properties:

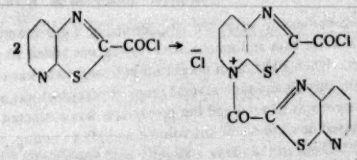


(I) (II)

Pyrido-(3,2-d)-thiazole has been especially closely studied. The following derivatives, for example, are known: 2-methyl-, 2-amino-, 2-hydroxy-, 2-mercapto-, 2-alkylmercapto-, and 2-chloropyrido-(3,2-d)-thiazoles and their 5- and 6-substituted derivatives [2]. However, pyrido-(3,2-d)-thiazole-2-carboxylic acid and pyrido-(3,2-d)-thiazole itself have not previously been described.

The objective of the present work was the synthesis of pyrido-(3,2-d)-thiazole-2-carboxylic acid and its amide, hydrazide and acylhydrazones. The starting compound for the synthesis of these derivatives is 2-methylpyrido-(3,2-d)-thiazole. Preparation of the latter was described by Japanese chemists in a difficultly accessible journal [3]. We had the opportunity of consulting this article which gives details of the preparation, boiling point and melting point of the compound. The 2-methylpyrido-(3,2-d)-thiazole that we prepared by this method was oxidized by potassium permanganate to pyrido-(3,2-d)-thiazole-2-carboxylic acid, and the acid was converted to the ester, amide, hydrazide and acylhydrazones by a scheme similar to that set forth in the preceding communication[1]. Decarboxylation of pyrido-(3,2-d)-thiazole-2-carboxylic acid gave the previously unknown pyrido-(3,2-d)-thiazole.

Pyrido-(3,2-d)-thiazole-2-carboxylic acid forms colorless needles(decomp. at 136°). Its acid chloride, like the acid chloride of pyrido-(3,4-d)-thiazole-2-carboxylic acid, was not isolated in the pure form. Attempts to recrystallize the acid chloride from benzene or ligroine led to its transformation into a compound with m.p. 186-187° whose nitrogen content corresponds to that of the acid chloride, but it does not form the anticipated methyl ester when boiled with methyl alcohol. This product is probably the result of interaction of two molecules of acid chloride according to the scheme:



Esters of pyrido-(3,2-d)-thiazole-2-carboxylic acid were obtained by boiling the unpurified acid chloride with methyl or ethyl alcohol. The amide of pyrido-(3,2-d)-thiazole-2-carboxylic acid is obtained by the action

of aqueous concentrated ammonia solution, while the hydrazide is formed by the action of hydrazine hydrate on the ester of this acid at room temperature.

The fact that the hydrazide is not obtained on heating indicates cleavage of the thiazole ring by hydrazine hydrate when heated. This phenomenon was also observed in the action of hydrazine hydrate on the methyl ester of pyrido-(3,4-d)-thiazole-2-carboxylic acid [1].

Acylhydrazones of pyrido-(3,2-d)-thiazole-2-carboxylic acid are readily formed and in quantitative yield.

The solubility in water and in organic solvents of derivatives of pyrido-(3,2-d)-thiazole is considerably lower than that of the corresponding derivatives of pyrido-(3,4-d)-thiazole, and the melting points are very much lower.

EXPERIMENTAL

2-Chloro-3-nitropyridine was the starting substance in the preparation of the 2-methylpyrido-(3,2-d)-thiazole that we needed. It was prepared by the action of phosphorus pentachloride on 2-hydroxy-3-nitropyridine [3], and the latter separated out of a mixture of isomers which formed upon nitration of 2-hydroxypyridine.

2-Hydroxypyridine was prepared by the method of A.E. Chichibabin and Shapiro [4] by diazotization of 2-aminopyridine. The solution of the diazo compound was neutralized with sodium carbonate until it gave a slightly acid reaction and was evaporated to dryness on a water bath. The dry residue was extracted with hot chloroform and, after driving off the chloroform, 2-hydroxypyridine distilled at 288°. Yield 83%, m.p. 105-106°, which corresponds to the literature data [4].

Nitration of 2-hydroxypyridine and separation of the isomeric nitro derivatives were carried out under the conditions described in the literature [5]; however, the yield cited by the authors for 2-hydroxy-3-nitropyridine was never reached by us.

3,3'-Dinitro-2,2'-dipyridyl disulfide was first prepared by Chichibabin and Woroshtzow [6] from 2-chloro-3-nitropyridine and potassium hydrosulfide in alcoholic solution. The compound had m.p. 202-205°. For the disulfide, synthesized by the same method, the literature cites m.p. 249-250° [3]. We prepared it from 2-chloro-3-nitropyridine and sodium disulfide. After crystallization from glacial acetic acid, our product had m.p. 203-205°. Evidently, the melting point given in the literature was erroneous.

2-Methylpyrido-(3,2-d)-thiazole was prepared by reducing the disulfide with zinc dust in acetic acid the same as in the case of 2-methylpyrido-(3,4-d)-thiazole. After driving off the chloroform, the residue was vacuum distilled, 120-123° at 12 mm. The literature data [3] give 118-120° (10 mm). Yield of distilled 2-methylpyrido-(3,2-d)-thiazole was 52%.

The hydrochloride was prepared by combining an ethereal solution of 2-methylpyrido-(3,2-d)-thiazole with an ethereal solution of hydrogen chloride. The salt was recrystallized from alcohol with ether. M.p. 188-189°.

Found %: N 14.50, 14.53. $C_7H_7N_2ClS$. Calculated %: N 15.01.

The picrate was prepared in alcoholic solution and recrystallized from a small quantity of alcohol. M.p. 150°.

Found %: N 18.31, 18.29; S 8.50, 8.70. $C_{13}H_9O_7N_5S$. Calculated %: N 18.47; S 8.44.

Pyrido-(3,2-d)-thiazole-2-carboxylic acid. To a suspension of 7 g 2-methylpyrido-(3,2-d)-thiazole in 250 ml water, with heating on a water bath and mechanical stirring, was added 20 g of finely ground potassium permanganate in small portions. When addition of potassium permanganate was complete, the mixture was heated for 30 minutes more with stirring and then several drops of perhydrol was added to decolorize the excess of permanganate. The hot mixture was filtered and the precipitate was extracted twice with hot water. The combined filtrates were evaporated down to 45-50 ml volume and, after cooling, the solution was carefully acidified with dilute hydrochloric acid until it gave a slightly acid reaction on Congo. The white precipitate which came down was filtered off after some time and then dissolved in a saturated solution of sodium carbonate; the solution was boiled with charcoal, filtered and precipitated with dilute hydrochloric acid. Yield 3.6 g (43%). M.p. 136° (decomp.).

Found %: N 15.47, 15.29; S 17.60, 17.73. $C_7H_4O_2N_2S$. Calculated %: N 15.55; S 17.77.

Methyl ester of pyrido-(3,2-d)-thiazole-2-carboxylic acid. 2 g pyrido-(3,2-d)-thiazolecarboxylic acid was mixed with 10 ml thionyl chloride and the mixture was heated on a water bath for 3 hours at 70-80°. Towards completion of heating a transparent solution formed. After driving off the excess of thionyl chloride, a liquid remained which crystallized upon cooling. To the crystalline mass was added 30 ml anhydrous methyl alcohol and the mixture was boiled on a water bath for 45 minutes. Alcohol was driven off from the resulting solution; the residue was covered with 15 ml saturated aqueous solution of sodium carbonate and the methyl ester of pyrido-(3,2-d)-thiazole-2-carboxylic acid was repeatedly extracted with chloroform. After driving off the chloroform, crystals remained which were recrystallized from ligroine. Yield 1.4 g (65%, on acid taken for reaction). M.p. 143°.

Found %: N 14.6, 14.37. $C_8H_6O_2N_2S$. Calculated %: N 14.43.

Ethyl ester of pyrido-(3,2-d)-thiazole-2-carboxylic acid was prepared in the same manner as the methyl ester. Yield 0.7 g (61%). It was recrystallized from ligroine. Light-yellow needles with m.p. 87°.

Found %: N 13.34, 13.60. $C_9H_8O_2N_2S$. Calculated %: N 13.46.

Amide of pyrido-(3,2-d)-thiazole-2-carboxylic acid. To 0.5 g methyl ester of pyridothiazolecarboxylic acid was added 10 ml concentrated aqueous ammonia solution and the mixture was set aside for 48 hours. The precipitate was filtered off and recrystallized from a large quantity of water. Yield 0.36 g (73%). Colorless needles with m.p. 289°.

Found %: N 23.20, 23.29. $C_7H_5ON_3S$. Calculated %: N 23.46.

Hydrazide of pyrido-(3,2-d)-thiazole-2-carboxylic acid. To a solution of 0.5 g methyl ester of pyrido-(3,2-d)-thiazole-2-carboxylic acid in 10 ml methyl alcohol was added 0.5 g hydrazine hydrate at room temperature. After 30 minutes, the precipitate which came down was filtered off, washed with methyl alcohol and recrystallized from ethyl alcohol. Yield 0.38 g (76%). Colorless needles, m.p. 258° (decomp.).

Found %: N 29.16, 29.11. $C_7H_6N_4S$. Calculated %: N 28.86.

Hydrazone with benzaldehyde. To a boiling solution of 0.2 g hydrazide of pyrido-(3,2-d)-thiazole-2-carboxylic acid in 5 ml glacial acetic acid was added a solution of 0.2 g benzaldehyde in 1 ml of the same acid and the mixture was boiled for 5 minutes. Upon cooling, 2 ml water was added, the precipitate of the hydrazone was filtered off and recrystallized from 150 ml alcohol. Yield 0.24 g (86%). Colorless needles with m.p. 261°.

Found %: N 19.39, 19.27. $C_{14}H_{10}ON_4S$. Calculated %: N 19.53.

Hydrazone with salicylaldehyde. It was prepared in the same manner as the preceding from 0.2 g hydrazide of pyrido-(3,2-d)-thiazole-2-carboxylic acid and 0.2 g salicylaldehyde. It was recrystallized from a large quantity of alcohol. Yield 0.27 g (90%). Colorless needles with m.p. 252°.

Found %: N 18.68, 18.62. $C_{14}H_{10}O_2N_4S$. Calculated %: N 18.79.

Pyrido-(3,2-d)-thiazole. 1 g pyrido-(3,2-d)-thiazole-2-carboxylic acid was heated in an open test tube on an oil bath at 160-175° for 10 minutes and then the contents of the test tube were extracted with boiling ligroine, the ligroine solution was boiled with charcoal, the solvent was driven off and the residue was recrystallized from petroleum ether. Yield 0.42 g (54%). Colorless needles with m.p. 53°.

Found %: N 20.50, 20.28. $C_6H_4N_2S$. Calculated %: N 20.58.

SUMMARY

1. Pyrido-(3,2-d)-thiazole-2-carboxylic acid, its methyl and ethyl esters, amide, hydrazide and two hydrazones were prepared.

2. Pyrido-(3,2-d)-thiazole was obtained by decarboxylation of pyrido-(3,2-d)-thiazole-2-carboxylic acid.

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DERIVATIVES OF BENZOTHIAZOLE

II. REACTION OF 2-BENZOTHIAZOLESULFONIC ACID WITH NITROGEN BASES

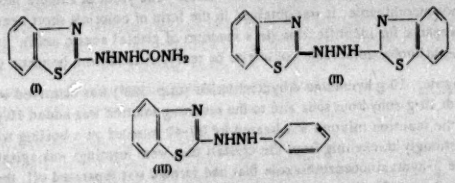
L. R. Davidenkov and B. A. Porai-Koshits

As was earlier reported [1], by heating potassium 2-benzothiazolesulfonate with aqueous solutions of ammonia, hydrazine and hydroxylamine, the sulfo group of 2-benzothiazolesulfonic acid is easily cleaved to give the corresponding electron-donating residues.

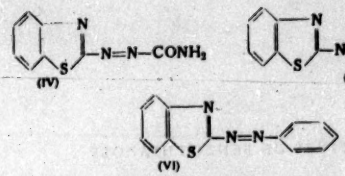
These facts gave grounds for suggesting that 2-benzothiazolesulfonic acid would react also with other nitrogen bases and that consequently many 2-derivatives of benzothiazole could be conveniently obtained by this route. We therefore decided to make a more detailed study of the reaction in question. For this purpose we investigated the interaction of 2-benzothiazolesulfonic acid with characteristic representatives of nitrogen bases: ammonia, methylamine, dimethylamine, aniline, methylaniline and diphenylamine; reactions with hydrazine, semicarbazide, phenylhydrazine, 2-hydrazinobenzothiazole and hydroxylamine were also investigated. In short, we took the simplest monosubstituted amine of the aliphatic series, the simplest disubstituted amine of the aliphatic series, and so on.

The experiments confirmed our ideas: in nearly all cases 2-benzothiazolesulfonic acid reacted according to the scheme proposed above. The reaction was conducted under fairly mild conditions and gave very good yields. However, 2-benzothiazolesulfonic acid did not react with methylaniline, diphenylamine or ethylaniline. The failure of 2-benzothiazolesulfonic acid to react with alkylanilines is extremely unexpected. 2-Chlorobenzothiazole which, in respect of susceptibility to substitution reactions, is entirely similar to 2-benzothiazolesulfonic acid, reacts with methylaniline [2] just as easily as with aniline [3]. As far as we know, the lack of reaction between 2-benzothiazolesulfonic acid and alkylanilines is the first observed case of a difference in the behaviors of the mobile sulfo group and of a mobile halogen atom in compounds with an aromatic character.

For confirmation of the structure of (benzothiazolyl-2)-semicarbazide-1 (I) and 2,2'-hydrazobenzothiazole (II), which have been obtained for the first time, and also of the structure of 2-phenylhydrazobenzothiazole (III), which has only been described in a patent [4], we subjected these compounds to oxidation:



In all cases we obtained azo products with the corresponding composition: benzothiazole azocarboxylic acid amide (IV), 2,2'-azobenzothiazole (V) and 2-phenyl azobenzothiazole (VI).



(IV) (V) (VI)

EXPERIMENTAL

2-Aminobenzothiazole. 6 g potassium 2-benzothiazolesulfonate (preparation previously described [1]) and 35 ml 25% aqueous solution of ammonia were heated in a sealed tube for 4 hours at 125°. Upon cooling, 2-aminobenzothiazole separated out, was washed on a filter with cold water and dried. Yield of impure substance was 65-70%. Recrystallized from benzene, 2-aminobenzothiazole was obtained in the form of leaflets with a pearly lustre and with m.p. 128° [5]. For its identification we prepared the picrate (in a medium of glacial acetic acid) with m.p. 265° [6].

2-Methylaminobenzothiazole. A solution of 4 g methylamine hydrochloride in 30 ml water was neutralized with 2.6 g anhydrous soda, then mixed with 6 g potassium 2-benzothiazosulfonate and the mixture was heated in a sealed tube for 3 hours at 115-120°. Upon cooling, the reaction mixture was rubbed in a mortar (2-methylaminobenzothiazole was obtained in the form of a flat cake), was sucked off from the liquid, washed on the filter with cold water and dried. Yield of impure 2-methylaminobenzothiazole 90-95%. Recrystallized from dilute ethyl alcohol (1:2) in the presence of activated carbon, it was obtained in the form of colorless leaflets with a pearly lustre with m.p. 138° [7].

Found %: N 17.26, 17.34. $C_8H_8N_2S$. Calculated %: N 17.07.

2-Dimethylaminobenzothiazole. 5 g dimethylamine hydrochloride, 3.4 g anhydrous soda, 6 g potassium 2-benzothiazolesulfonate and 30 ml water were heated for 3 hours at 130°. Yield of impure product was 85-90%. It is most efficient to purify it by vacuum distillation (less efficient is recrystallization from gasoline). 2-Dimethylaminobenzothiazole was obtained in the form of colorless coarse crystals with m.p. 87° [8]. It must be noted that the method of purifying 2-dimethylaminobenzothiazole (crystallization from a small quantity of ethyl alcohol) that the literature recommends is completely ineffective according to our data.

Found %: C 60.55, 60.74; H 5.44, 5.51. $C_9H_{10}N_2S$. Calculated %: C 60.67; H 5.62.

2-Anilinobenzothiazole. A mixture of 4 g potassium 2-benzothiazosulfonate, 2.3 ml aniline and 16 ml water was heated in a sealed tube for 3 hours at 130°. Upon cooling, crystals of 2-anilinobenzothiazole separated out from the liquid, were washed on a filter with cold water and then with several portions of dilute ethyl alcohol (1:1). The latter operation was carried out until the alcoholic filtrate did not become turbid upon dilution with water. 2-Anilinobenzothiazole was further dried. The yield of impure product was 65-70%. Recrystallized from 2-anilinobenzothiazole, it was obtained in the form of colorless short needles with m.p. 158° [9]. The picrate was prepared for identification (in a medium of glacial acetic acid); it had m.p. 224° [2]. It must be noted that 2-anilinobenzothiazole could also be recrystallized from benzene or alcohol.

2-Hydrazinobenzothiazole. 10 g hydrazine dihydrochloride (m.p. 198°) was dissolved with heating in 40 ml water, neutralized with 10 g anhydrous soda and to the resulting solution was added 10 g potassium 2-benzothiazolesulfonate and the reaction mixture was heated for 30-40 minutes on a boiling water bath. Upon cooling, the reaction mass (strongly thickening from the crystals that were forming) was agitated with water, transferred to a filter and the 2-hydrazinobenzothiazole that had formed was separated off, thoroughly washed with cold water and dried at about 80°. The yield of impure substance was 90-95%. Recrystallized from dilute ethyl alcohol (1:1) in presence of activated carbon, it was obtained in the form of colorless acicular crystals with m.p. 197°. The substance had to be stored in the dark.

Instead of hydrazine dihydrochloride and soda, an equivalent quantity of hydrazine hydrate may be used successfully. However, use of hydrazine sulfate results in failure.

(Benzothiazolyl-2)-semicarbazide-1. A hot solution of 10.6 g semicarbazide hydrochloride in 50 ml hot water, neutralized with 4 g anhydrous soda*, was poured in a small flask fitted with reflux condenser. To this was added 12 g potassium 2-benzothiazosulfonate and the whole mass was boiled with continuous mechanical stirring for 25-30 minutes. Upon cooling, the product that formed was sucked off, washed on a filter with cold water and dried. The yield of impure substance was 75-80%. Recrystallized from large amounts of ethyl alcohol, (benzothiazolyl-2)-semicarbazide was obtained in the form of fine colorless crystals with m.p. 217°. Dilute solutions of benzothiazolyl semicarbazide in solvents assume an intense blue color under the action of caustic alkalis.

Found %: N 27.21, 27.10; S 15.13, 15.58. $C_8H_9ON_4S$. Calculated %: N 26.90; S 15.38.

Amide of benzothiazole azocarboxylic acid**. To a suspension of 2 g benzothiazolylsemicarbazide in 300 ml boiling water with stirring was added a hot solution of 1 g potassium permanganate in 20 ml hot water acidified with 6 ml 1 N sulfuric acid. The resulting orange liquid was rapidly filtered off while hot from the manganese residue and set aside to cool slowly. Upon cooling, the crystalline precipitate of benzothiazole azocarboxylic acid amide was separated off, washed on a filter with cold water and dried. The yield was 70-75%. Recrystallized from glacial acetic acid, benzothiazole azocarboxylic acid was obtained in the form of brick-red acicular crystals with m.p. 173°.

Found %: N 27.40, 27.46. M 210, 205 (in dioxane***). $C_8H_6ON_4S$. Calculated %: N 27.18; M 206.

2-Phenylhydrazobenzothiazole. A mixture of 10 g recrystallized potassium 2-benzothiazolesulfonate, 8.5 ml distilled phenylhydrazine and 30 ml water was heated for 2-3 hours on a boiling water bath. Upon cooling, the reaction mass (strongly thickened from the crystals that formed) was agitated with water, placed on a filter and further treated the same as in the case of 2-anilinobenzothiazole. The yield of quite pure product was 70-75%. Recrystallized from a large quantity of ethyl alcohol, 2-phenylhydrazobenzothiazole was obtained in the form of fine needles with m.p. 227° [4].

It must be noted that the yield was greater when the synthesis of 2-phenylhydrazobenzothiazole was carried out in sealed tubes at 130°.

Found %: N 17.68, 17.45. $C_{14}H_{11}N_3S$. Calculated %: N 17.43.

2-Phenyl azobenzothiazole. A mixture of 2 g 2-phenylhydrazobenzothiazole, 5 g mercuric oxide and 40 ml ethyl alcohol was boiled for 10-15 minutes. (To moderate the boiling it was necessary to use bits of unglazed porcelain.) The reaction mixture, while hot, was then filtered; the filtrate was diluted with a small quantity of hot water and set aside to cool slowly. Upon cooling, 2-phenyl azobenzothiazole was separated off and dried. The yield of sufficiently pure product was 75-80%. Recrystallized from dilute acetic acid (2:1), it was obtained in the form of orange needles with m.p. 142°.

Found %: N 17.88, 17.68. M 222, 235. $C_{13}H_9N_3S$. Calculated %: N 17.57. M 239.

2,2'-Hydrazobenzothiazole. 4 g 2-hydrazinobenzothiazole was rubbed in a mortar with 6 g potassium 2-benzothiazolesulfonate and then this mixture together with 25 ml water was heated in a sealed tube for 3 hours at 140-150°. Upon cooling, the reaction mass was separated off from the liquid, washed on a filter with cold water and then twice agitated with some dilute hydrochloric acid (1:4) and twice filtered from the acid solution. Finally, the completely washed product was dried. Yield of impure 2,2'-hydrazobenzothiazole was 30-35%. Its purification was accomplished by recrystallization from aniline with subsequent washing with benzene on a filter. 2,2'-Hydrazobenzothiazole was thus obtained in form of fine colorless needles, having the form of a belt-like mass. The substance had to be stored, in the dark. We failed to determine the melting point, since upon heating, the substance gradually was converted to 2,2'-azobenzothiazole (judging by the corresponding color reaction, see below).

Although 2,2'-hydrazobenzothiazole is noted in the reference journals as a known compound, in its original source [11] its constants are not given. Evidently, this structure was ascribed without verification, to the (insoluble in dilute acids) reaction product of 2-chlorobenzothiazole with hydrazine hydrate.

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* In this synthesis the soda was taken in insufficient quantity (4 g instead of 5) since otherwise the synthesis is usually unsuccessful.

** Compare preparations of amide of benzene azocarboxylic acid [10].

*** Value of cryoscopic constant for dioxane (4.7) [13].

Found %: N 18.76, 18.68; S 21.70, 21.63. $C_{14}H_{10}N_4S_2$. Calculated %: N 18.79; S 21.48.

2,2'-Azobenzothiazole. A mixture of 0.4 g 2,2'-hydrazobenzothiazole, 1.6 g mercuric oxide and 12 ml chlorobenzene was boiled for 5-10 minutes and then the still hot liquid was filtered. Upon cooling, the 2,2'-azobenzothiazole which came down was separated off and dried. A very pure product was obtained which was in the form of fine cherry-red needles with m.p. 294° (295°) [12]. The substance crystallized from chlorobenzene. The action of concentrated KOH solution colored an alcoholic solution of 2,2'-azobenzothiazole dark-green. Upon subsequent dilution with water, the initial color returned.

Found %: N 19.12, 19.08. $C_{14}H_8N_4S_2$. Calculated %: N 18.92.

SUMMARY

1. 2-Benzothiazolesulfonic acid reacts with facility with various nitrogen bases. With a few exceptions, this reaction is a very convenient method of synthesis of many 2-derivatives of benzothiazole.

2. For the first time an example was observed of differing behaviors of the mobile sulfo group and of the mobile halogen atom in compounds of aromatic character: 2-chlorobenzothiazole reacts with aniline and with methylaniline, but 2-benzothiazolesulfonic acid reacts only with aniline.

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TAUTOMERIC COMPOUNDS

XXI. TAUTOMERISM OF DERIVATIVES OF DIPYRAZOLONYL-PHENYL-METHANE

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In an earlier communication [1] careful consideration was given to the problem of the structure and transformations of dipyrazolonyl-m-nitrophenylmethanes. It was found that the reciprocal transformations of white and yellow dipyrazolonyl-m-nitrophenylmethanes are an example of keto-enol tautomerism, the white product being the enol and the yellow one the keto form.

In the present communication we examine the influence of the character and position of the substituent in the aldehyde residue upon the tautomerism of dipyrazolonyl-aryl-methanes. We selected for investigation dipyrazolone derivatives of benzaldehyde, o-, m- and p-nitrobenzaldehydes, and their chloro and hydroxy analogs.

Employing the methods of preparation of the white and yellow products developed for dipyrazolonyl-m-nitrophenyl-methanes, we condensed 1-phenyl-3-methyl-pyrazolone-5 with all the above-mentioned aldehydes. During the experiments we found that products of condensation of the pyrazolone with aldehydes substituted in the m-position can be obtained and separated with greater ease than the others. The tautomeric products obtained exhibit marked differences in melting points and properties:

Initial aldehyde	Melting point of white product	Melting point of yellow product
m-Nitrobenzaldehyde	150°	227°
m-Chlorobenzaldehyde	149°	216°
m-Hydroxybenzaldehyde	181°	152°

Isolation of the two forms is impeded when substituents are in the ortho- and para-positions of the aldehyde residue: the difference in their melting points is lower, one of the products has reduced stability, and, for example, in the case of o- and p-chlorobenzaldehydes only one form could be separated in each case.

Initial aldehyde	Melting point of white product	Melting point of yellow product
o-Nitrobenzaldehyde	172°	225°
p-Nitrobenzaldehyde	217°	227°
o-Hydroxybenzaldehyde	226°	223°
p-Hydroxybenzaldehyde	162°	216°
o-Chlorobenzaldehyde	231°	Not detected
p-Chlorobenzaldehyde	208°	"
Benzaldehyde	174°	"

Determination of the elementary compositions and molecular weights of the white and yellow products shows that they are completely identical.

The reciprocal transitions of the white and yellow products are analogous to the reciprocal transitions of the white and yellow dipyrazolonyl-m-nitrophenyl-methanes. The identity of the molecular weights and elementary compositions of the white and yellow products, together with the reciprocal transitions of the latter,

*Deceased.

give grounds for assuming that each separated pair of products is a tautomeric pair. From a consideration of the behavior of the white and yellow substances and their complete analogy with the dipyrazolonyl-m-nitrophenylmethanes, we reached the conclusion that all the white products are enolic tautomers and all the yellow products ketonic tautomers.

Concerning the stability of one tautomeric form or the other, it depends upon the position and nature of the substituent in the aldehyde residue: a) a substituent in the meta-position promotes the stability of both tautomers, substituents in the ortho- and para-positions promote the stability of one of the forms; b) a nitro group promotes the stability of the ketonic tautomer, while hydroxy and p-chloro groups promote stability of the enolic tautomers. As already indicated, we were quite unable to separate the yellow products in the case of o- and p-chlorobenzaldehydes. The same is true of the derivative of unsubstituted benzaldehyde.

EXPERIMENTAL

1. Reaction of 1-phenyl-3-methylpyrazolone-5 with o-nitrobenzaldehyde*

Preparation of yellow product. To a solution (heated to 40-50°) of 0.01 mole pyrazolone (in 96% ethyl alcohol) was added 0.005 mole o-nitrobenzaldehyde. Upon strong cooling and rubbing with a rod, after several hours from the red solution there came down a yellow finely crystalline precipitate which had m.p. 225°. Quantitative yield.

Found %: C 66.97, 67.10; H 4.58, 4.60; N 14.62, 14.22. M 478 (according to Rast). $C_{27}H_{22}O_4N_5$. Calculated %: C 67.36; H 4.78; N 14.55. M 481.

The product was insoluble in water and many organic solvents: alcohol, benzene, ligroine; it was difficultly soluble in acetone and in acetic acid; it was soluble when heated in dilute alkali, ammonia and in pyridine.

Preparation of the white product. 1 g obtained yellow product (m.p. 225°) was dissolved with heating in 5 ml 10% aqueous solution of caustic soda and the resulting red solution was neutralized with 10% acetic acid. A white precipitate came down which was rapidly filtered off, washed with water and dried in a vacuum desiccator to constant weight over sulfuric acid. M.p. 172°. Yield 0.95 g. The product was very unstable: even during drying it colored red on the surface. Upon recrystallization from anhydrous alcohol, the product assumed a faintly yellowish tinge and had m.p. 203-205°. Upon keeping the recrystallized product in a weighing bottle for several days, the melting point of the product rose to 225°.

Upon consideration of the tendency of the product with m.p. 203-205° to quantitatively convert to the yellow product (m.p. 225°) upon long standing, we supposed that the first was a mixture of white (m.p. 172°) with yellow (m.p. 225°) products, i.e., a mixture of 4,4'-di-(1-phenyl-3-methyl-5-hydroxy)-pyrazolyl-(2''-nitrophenyl)-methane and 4,4'-di-(1-phenyl-3-methyl)-pyrazolonyl-(2''-nitrophenyl)-methane. Analysis of product (m.p. 203-205°):

Found %: C 67.23; H 4.70; N 14.50. $C_{27}H_{22}O_4N_5$. Calculated %: C 67.37; H 4.78; N 14.55.

The agreement in the analytical results on the elementary compositions of the product with m.p. 203-205° and the yellow (m.p. 225°) product leads us to believe that the white product corresponds in composition to the yellow.

2. Reaction of 1-phenylmethylpyrazolone-5 with m-hydroxybenzaldehyde.

Preparation of the white product. To a solution (heated to 40-50°) of 0.01 mole phenylmethylpyrazolone in 10 ml 96% alcohol was added 0.005 mole m-hydroxybenzaldehyde. After 24 hours, a white crystalline product came down from the orange solution; it had m.p. 179°. Yield 85%. Upon dilution of the filtrate with water, a small additional quantity of product came down with m.p. 177°. After 3 recrystallizations from 96% ethyl alcohol, it had m.p. 181°.

Found %: C 71.65, 71.60; H 5.26, 5.28; N 12.60, 12.69. M 451.5 (potentiometric titration). $C_{27}H_{24}O_3N_4$. Calculated %: C 71.68; H 5.34; N 12.39. M 452.

* The data on the reaction of 1-phenyl-3-methylpyrazolone-5 with m- and p-nitrobenzaldehyde are given in Communication VII [2].

Preparation of yellow product. a) To a solution of 0.01 mole pyrazolone in 70% acetic acid was added 0.005 mole m-hydroxybenzaldehyde and the resulting mixture was boiled on a sand bath for 15-20 minutes in a small flask fitted with reflux condenser. Upon slow cooling of the solution on a cooling water bath, the yellow product with m.p. 150° crystallized out. Yield of crude product 94%. After 2-fold recrystallization from 70% acetic acid, it had m.p. 152°.

b) A suspension of 1 g white product (m.p. 181°) in 20 ml 96% ethyl alcohol was boiled for 30 minutes in a flask fitted with reflux condenser. In the process of boiling, the precipitate dissolved and came down again as a yellow product. M.p. 150°. The yield was quantitative. After recrystallization from 70% acetic acid, it had m.p. 152°.

Found %: C 71.30, 72.00; H 5.45, 5.12; N 12.68, 12.30. $C_{27}H_{24}O_3N_4$. Calculated %: C 71.68; H 5.34; N 12.39.

The product was in the form of yellow flakes, soluble with heating in alcohol and acetic acid. It was readily soluble in acetone, pyridine and in alkalis. Upon acidification of the alkaline solutions, a white product came down with m.p. 177-179°.

3. Reaction of 1-phenyl-3-methylpyrazolone-5 withp-hydroxybenzaldehyde.

Preparation of white product. We started with 0.01 mole pyrazolone and 0.005 mole aldehyde, which were condensed as in the preparation of white product from m-hydroxybenzaldehyde. Product had m.p. 162°. Yield 85%. After recrystallization from anhydrous alcohol, it had m.p. 162°.

Found %: C 71.2; H 5.24; N 12.28. M 451 (potentiometric titration). $C_{27}H_{24}O_3N_4$. Calculated %: C 71.68; H 5.34; N 12.39. M 452.

In its properties the white product was similar to the white product prepared from m-hydroxybenzaldehyde.

Preparation of yellow product. 0.01 mole pyrazolone was condensed with 0.005 mole aldehyde by the methods described in the preparation of the yellow product from m-hydroxybenzaldehyde (Items "a" and "b"). In both cases a yellow product was obtained with m.p. 214° with yields of 85% in the first case and a quantitative yield in the second case. After three recrystallizations from 70% acetic acid, the product had m.p. 216°.

Found %: C 71.60; H 5.25; N 12.29. M 448 (Rast). $C_{27}H_{24}O_3N_4$. Calculated %: C 71.68; H 5.34; N 12.39. M 452.

The yellow product was similar in properties to the yellow product prepared from m-hydroxybenzaldehyde. However, in contrast to the latter, it was not stable in solutions; in alcohol it readily converted to the white product, in acid solutions it decomposed with cleavage of phenylmethylpyrazolone and formation of the monoarylidene derivative – "the red product" [2]. A similar cleavage to pyrazolone and "red product" occurred also upon long standing of the yellow product in the air.

4. Reaction of 1-phenyl-3-methylpyrazolone-5 with o-hydroxybenzaldehyde.

Preparation of the white product. We started from 0.01 mole pyrazolone and 0.005 mole of aldehyde. The reaction was carried out by the method cited for the preparation of the white product from m-hydroxybenzaldehyde. A white product formed with m.p. 220°. Yield of product 80%. After several recrystallizations from anhydrous alcohol, the product had m.p. 226°.

Found %: C 71.70; H 5.28; N 12.49. M 451 (potentiometric titration). $C_{27}H_{24}O_3N_4$. Calculated %: C 71.68; H 5.34; N 12.39. M 452.

In its properties, the product was similar to the white product prepared from m-hydroxybenzaldehyde.

Preparation of the yellow product. We started from 0.5 g white product, which was boiled for 10-15 minutes with 10 ml 70% acetic acid. The solution that was filtered off from the insoluble portion was left to cool on a cooling water bath: a yellow product came down which had m.p. 223° and in properties was similar to the yellow product from p-hydroxybenzaldehyde.

Found %: C 71.30; H 5.42; N 12.50. M 444 (Rast). $C_{27}H_{24}O_3N_4$. Calculated %: C 71.68; H 5.34; N 12.39. M 452.

5. Reaction of 1-phenyl-3-methylpyrazolone with m-chlorobenzaldehyde.

Preparation of the white product. 0.01 mole pyrazolone was condensed with 0.005 mole aldehyde similarly to the condensation of pyrazolone with m-hydroxybenzaldehyde. After 24 hours and upon rubbing with a rod, a white crystalline precipitate came down which had m.p. 146°. Yield 98%. After 3 recrystallizations from 96% ethyl alcohol, it had m.p. 149°.

Found %: Cl 7.40, 7.29; N 12.02. M 468 (potentiometric titration). $C_{27}H_{23}O_2N_4Cl$. Calculated %: Cl 7.55; N 11.89. M 471.

The product was soluble in caustic and carbonate alkalis, insoluble in benzene, toluene, xylene, soluble with heating in alcohol and acetic acid and also soluble in acetone and concentrated sulfuric acid.

Preparation of the yellow product. 0.01 mole pyrazolone and 0.005 mole m-chlorobenzaldehyde was condensed according to the method described in Item "a" for the preparation of the yellow product from m-hydroxybenzaldehyde. A product formed with m.p. 214-215°. The yield of product was 68%. After 3 recrystallizations from 70% acetic acid, it had m.p. 216°.

Found %: Cl 7.36; N 12.03. M 460 (Rast). $C_{27}H_{25}O_2N_4Cl$. Calculated %: Cl 7.55; N 11.89. M 471.

The product was insoluble in most organic solvents and was soluble only in acetic acid and with heating in alcohol and in acetone. Upon heating, it was soluble in caustic alkalis and upon acidification of the alkaline solutions, a precipitate of the white product with m.p. 148° came down.

6. Reaction of 1-phenyl-3-methyl-5-pyrazolone with p-chlorobenzaldehyde.

Preparation of the white product. We started from 0.01 mole pyrazolone and 0.005 mole aldehyde, which was condensed by the method described for the preparation of the analogous product from m-chlorobenzaldehyde. After 24 hours and upon rubbing with a rod, a quantitative yield of white product came down with m.p. 204°. After several recrystallizations from 96% ethyl alcohol, the product had m.p. 208°.

Found %: N 11.95, 12.09; Cl 7.45. M 463 (potentiometric titration). $C_{27}H_{23}O_2N_4Cl$. Calculated %: N 11.90; Cl 7.55. M 471.

In properties it was similar to the white product from m-chlorobenzaldehyde. The yellow product could not be obtained; all attempts to prepare it resulted in the white product (m.p. 204-208°).

7. Reaction of 1-phenyl-3-methyl-pyrazolone-5 with o-chlorobenzaldehyde.

Preparation of the white product. 0.01 mole pyrazolone was condensed with 0.005 mole freshly-prepared aldehyde according to the method described for the preparation of the white product from m-chlorobenzaldehyde. A cream-colored product formed which had m.p. 223°. After 3 recrystallizations, the product whitened and had m.p. 231°.

Found %: N 12.01; Cl 7.66. M 468 (potentiometric titration). $C_{27}H_{23}O_2N_4Cl$. Calculated %: N 11.90; Cl 7.55. M 471.

In properties the product was similar to the white product from m-chlorobenzaldehyde. As in the case of the reaction with p-chlorobenzaldehyde, the yellow product could not be isolated.

8. Reaction of 1-phenyl-3-methylpyrazolone-5 with benzaldehyde.

Preparation of the white product. We started from 0.01 mole pyrazolone and 0.005 mole freshly-distilled aldehyde which was condensed according to the method described for the preparation of the white product from m-hydroxybenzaldehyde. A white product formed with m.p. 165-166° in an almost quantitative yield (99.8%). After many recrystallizations from 96% alcohol, the product had m.p. 174°.

Found %: C 74.25; H 5.58; N 13.01. $C_{27}H_{24}O_2N_4$. Calculated %: C 74.30; H 5.51; N 12.84.
The molecular weight was determined by the method of potentiometric titration. Found: M 433.5. $C_{27}H_{24}O_2N_4$. Calculated: M 436.

The product was in the form of well formed crystals. It was soluble in alkalis and pyridine and also in acetone, concentrated sulfuric acid; upon heating, it was soluble in alcohol and concentrated acetic acid. The yellow product could not be isolated.

SUMMARY

1. Products of condensation of various aldehydes of the benzene series with 1-phenyl-3-methylpyrazolone-5 – dipyrazolyl-arylmethanes – are susceptible to tautomeric transformations of the keto-enol type.

2. In the majority of the cases the ketones and enols can be isolated in the form of stable compounds which change into one another under specific conditions.

3. The character of the aldehyde residue influences the stability of one tautomeric form or the other.

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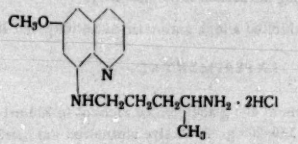
CHEMICAL STRUCTURE AND PARASITICIDAL ACTIVITY

XIX. SYNTHESIS OF 6-METHOXY-8-(4'-AMINOPENTYL)-AMINOQUINOLINE

M. B. Braude and V. I. Stavrovskaya

Among the numerous derivatives of 6-methoxy-8-aminoquinoline there are relatively few compounds with a primary amino group in the side "chain" [1-14]. Biological tests of the latter revealed high antimalarial activity by some members, although without appreciable advantage over analogous compounds containing a diethylamino group in the alkylamine. An exception is 6-methoxy-8-4'-amino-1'-methylbutyl)-aminoquinoline "primaquine" [11,15], tests on which in connection with avian malaria revealed an activity higher than that of plasmochin [16]. Employment of primaquine in combination with quinine led moreover to a considerable fall in the number of relapses in three-day malaria [17].

The new antimalarial preparation 6-methoxy-8-(4'-aminopentyl)aminoquinoline dihydrochloride ("chinocid"),



which differs from primaquine in respect of the structure of the side chain, was obtained by reaction of 6-methoxy 8-aminoquinoline with 2-amino-5-bromopentane hydrobromide. The starting substance for synthesis of the latter was acetopropyl alcohol, reductive amination of which gave 2-aminopentanol-5 [18] (we succeded in raising the yield from 46% to 75%). The aminopentanol was converted into 2-amino-5-bromopentane by treatment with thionyl bromide or hydrobromic acid.

In the reaction of 6-methoxy-8-aminoquinoline with haloalkylamines, the amino groups of the latter are usually protected by the phthalimide residue. Reaction between 6-methoxy-8-aminoquinoline and haloalkylamines with an unprotected primary amino group, as described for the synthesis of primaquine [11], proceeds with a yield of 14-28% due to a secondary reaction of cyclization of the haloalkylamine.

Applying the latter method to the synthesis of "chinocid" from 6-methoxy-8-aminoquinoline and the hydrobromide of 2-amino-5-bromopentane, we obtained an end-product yield of 17-30% (although it fell to 7% and even to 2.7% in a strongly acid medium). The yield was not improved by increasing the proportion of 2-amino-5-bromopentane hydrobromide to 2 moles per mole of 6-methoxy-8-aminoquinoline or by lowering the proportion of the latter to 1 mole per mole of bromoalkylamine (Table 1).

Numerous experiments on the synthesis of chinocid by simultaneous introduction of the components (regardless of the duration of heating but not less than 1 hour) showed (Table 2) that about 60% of unreacted 6-methoxy-8-aminoquinoline was usually recovered from the reaction, while 2-amino-5-bromopentane underwent cyclization.

TABLE 1

Preparation number	6-Methoxy-8-aminoquinoline (in moles)	2-Amino-5-bromopentane hydrobromide (in moles)	Yield of chinocid (base) (in %)	Unreacted 6-methoxy-8-aminoquinline (%)
1	1	1	30.1	56
2	2	1	24.7	62
3	1	2	19.7	53

TABLE 2

Preparation no.	Duration of heating (hours)	Yield of chinocid (base) (in %)	6-Methoxy-8-aminoquinoline not entering into reaction (in %)
1	12	30.8	57.5
2	6	31.1	58.8
3	3	30.1	56.0
4	2	30.8	59.8
5	1	33.5	58.6

Note. The starting substances were taken in molar ratio.

On the basis of the results obtained, we succeeded in reducing the duration of heating to 2-4 hours (instead of 13 hours in the synthesis of primaquine) and in raising the yield of chinocid to 45-62.9% (calculated on the amount of 6-methoxy-8-aminoquinoline taken into the reaction) by supplementary portionwise addition of 2-amino-5-bromopentane hydrobromide to 1 mole of 6-methoxy-8-aminoquinoline, the first portion of starting substances, taken in molar ratio, being introduced simultaneously.

In biological tests chinocid exhibited a high antimalarial activity, not inferior to that of primaquine *.

EXPERIMENTAL

2-Aminopentanol-5. A solution of 400 g acetopropyl alcohol in 200 ml water was saturated with gaseous ammonia until a weight addition of 180-200 g. Reductive amination was carried out at room temperature and 2 atm. hydrogen pressure in presence of nickel catalyst. When absorption of hydrogen was complete, the solution was filtered off from the catalyst, the filtrate was acidified with concentrated hydrochloric acid until acid reaction and then evaporated down in vacuum until water stopped coming off. The residue – a mixture of crystals with darkly colored viscous liquid – was dissolved in alcohol, crystalline precipitate of ammonium chloride was filtered off and washed (alcohol). The alcohol was driven off in vacuum, to the residue was added a 40% solution of caustic soda until all the dark oil had separated out on the surface; the latter was extracted with chloroform. The chloroform solution was dried with potash; after the solvent was removed, the residue was vacuum-distilled at 86° (4 mm). Yield 302 g (74.7%). It was a colorless liquid which crystallized upon cooling, m.p. 32°.

2-Amino-5-bromopentane. 2-Aminopentanol-5 (310 g) and 48% hydrobromic acid (930 g) was heated for 5 hours at a calcium chloride bath temperature of 120-125°. The excess of hydrobromic acid was vacuum distilled. To the residue of non-crystallizing brown viscous liquid was added hydrobromic acid (310 g) and the solution was heated again for 2 hours. The excess of hydrobromic acid was removed in vacuum. Upon cooling, the residue solidified. Yield 737 g (99.1%) of 2-amino-5-bromopentane hydrobromide.

The hydrobromide of 2-amino-5-bromopentane was readily soluble in water, alcohol, acetone, chloroform, insoluble in ether and benzene. It purified by solution in acetone with subsequent precipitation with ether. Colorless crystals, m.p. 96-97°.

Found %: N 5.85, 5.74. $C_5H_{13}NBr_2$. Calculated %: N 5.67.

6-Methoxy-8-(4'-aminopentyl)-aminoquinoline

* Thanks are conveyed to Sh. D. Moshkovsky and S. A. Syrkina for carrying out the biological tests.

a) 6-Methoxy-8-aminoquinoline (261 g), 2-amino-5-bromopentane (371 g) and 260 ml water were heated for 2 hours with stirring at a temperature of 102-104° of the reaction liquid. Upon completion of heating, 780 ml boiling water was added and the solution was acidified with concentrated hydrochloric acid until the reaction was acid on Congo. A mixture of the hydrochloride and hydrobromide of 6-methoxy-8-aminoquinoline which came down upon cooling the solution to 5° was separated off and washed with ice water; to the filtrate was added a solution of sodium acetate and the remaining 6-methoxy-8-aminoquinoline was extracted with ether. The aqueous layer was alkalized with 20% caustic soda solution and extracted with ether; the ethereal solution was washed with water and dried with potash. After driving off the ether, the residue was vacuum distilled at b.p. 183-186° (1 mm). Yield 124 g (31.9%).

The base was a light-yellow oil with a green fluorescence. It solidified upon cooling, m.p. 46°. It was readily soluble in alcohol, ether, benzene.

Found %: C 69.80, 69.52; H 8.16, 8.23; N 15.95, 16.10. $C_{15}H_{21}ON_3$. Calculated %: C 69.50; H 8.10; N 16.2.

6-Methoxy-8-(4'-aminopentyl)-aminoquinoline hydrochloride was prepared by running alcoholic hydrochloric acid into a solution of the base in anhydrous alcohol. The hydrochloride which came down was crystallized from anhydrous alcohol, m.p. 227-227.5°. It was readily soluble in water.

Found %: C 54.18, 54.52; H 7.04, 7.13; N 12.92, 12.94. $C_{15}H_{21}ON_3 \cdot 2HCl$. Calculated %: C 54.21; H 6.90; N 12.65.

The unreacted filtered-off mixture of hydrochloride and hydrobromide of 6-methoxy-8-aminoquinoline was dissolved in water, alkalized with 20% solution of caustic soda and the resulting base of 6-methoxy-8-aminoquinoline was extracted with ether. The ethereal solution was added to an ethereal solution of 6-methoxy-8-aminoquinoline, prepared previously by extracting a solution, neutralized with sodium acetate. After drying over potash, ether was driven off and 6-methoxy-8-aminoquinoline was vacuum distilled. B.p. 149-163° (1 mm). Yield 144 g (55.1%).

b) 6-Methoxy-8-aminoquinoline (17.4 g), 2-amino-5-bromopentane (24.7 g) and 18 ml water were heated with stirring for 1 hour at temperature 102° of the liquid. The reaction liquid was brought to a weakly acid reaction by a solution of potash and then to it was added the hydrobromide of 2-amino-5-bromopentane (14.8 g). Heating was complete within one hour after introduction of the additional quantity of 2-amino-5-bromopentane. The reaction mass was diluted with 54 ml boiling water and was acidified with hydrochloric acid until it gave an acid reaction on Congo. Further treatment was as in the preceding experiment. The base was distilled in vacuum. B.p. 213-216° (3 mm). Yield 11.7 g (45%).

c) 6-Methoxy-8-aminoquinoline (17.4 g), 2-amino-5-bromopentane hydrobromide (24.7 g) and 18 ml water were heated with stirring for 1 hour at a temperature of 102° of the liquid. A solution of potash was then added until the reaction was weakly acid and 2-amino-5-bromopentane (14.8 g) was added. After 1 hour, potash was again added to the reaction mass, 2-amino-5-bromopentane (8.9 g) was added and the reaction mass was heated for 1 hour. The reaction mass was neutralized by a solution of potash for the 3rd time and 2-amino-5-bromopentane (5.3 g) was added. Heating was complete 1 hour after addition of the last portion of 2-amino-5-bromopentane hydrobromide. Further treatment was as in the preceding experiment; b.p. of base 183-187° (1 mm). Yield 16.3 g (62.9%).

Synthesis of "Chinocid" in strongly acidic medium.

a) To a solution of 24.7 g 2-amino-5-bromopentane in 18 ml water, heated to 100°, with stirring was added 17.4 g 6-methoxy-8-aminoquinoline base (in 2-g portions after each 15 minutes). Within 1 hour after addition of the last portion of 6-methoxy-8-aminoquinoline, heating was halted. The reaction mass was diluted with 54 ml water and acidified with hydrochloric acid. Further treatment was according to the above-described method. The base was distilled at b.p. 221-227° (5 mm). The yield was 2 g (7.72%). 14.7 g (67.1%) 6-methoxy-8-aminoquinoline with b.p. 163-165° (2 mm) was returned.

b) 25.5 g 6-methoxy-8-aminoquinoline, 24.7 g 2-amino-5-bromopentane and 18 ml water were heated for 6 hours at 102-104°. The reaction mass was treated in the usual way. A base was obtained with b.p. 239° (4 mm). Yield 0.7 g (2.7%). 17 g (66.7%) of unreacted 6-methoxy-8-aminoquinoline hydrobromide was separated.

SUMMARY

1. A new antimalarial substance, 6-methoxy-8-(4'-aminopentyl) aminoquinoline ("chinocid"), was synthesized and characterized, and a procedure for its preparation was developed.

2. Transfer of the methyl group from position 1 to position 4 in the side chain of 6-methoxy-8-(4'-aminopentyl) aminoquinoline did not lower the antimalarial activity.

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SULFONATION AND SULFONIC ACIDS OF ACIDOPHOBIC COMPOUNDS

XXVI. USE OF DIOXANE–SULFOTRIOXIDE FOR THE DETERMINATION OF AROMATIC AMINES AND ALDEHYDES

A. P. Terentyev, N. B. Kupletskaya and E. V. Andreeva

In the preceding communication [1] a method was described for the determination of hydroxyl groups in various hydroxy compounds based upon the quantitative formation of sulfuric acid esters on reaction of hydroxy compounds with dioxane-sulfotrioxide.

As we know, amines likewise react with dioxane-sulfotrioxide with formation of the corresponding sulfamic acids [2]:

$$RNH_2 + O(CH_2CH_2)_2O \cdot SO_3 \rightarrow RNHSO_3H + O(CH_2CH_2)_2O.$$

The reaction goes rapidly and quantitatively.

We thought it might be possible to utilize this reaction for analysis of amino compounds by determining, as in the case of alcohols, the change of titer of the solution after reaction with a weighed sample of the substance in question. Of course there is no special point in employing dioxane-sulfotrioxide in the case of strong bases (aliphatic amines) since the latter are satisfactorily determined by titration with acids.

We made use of this method for aromatic amines which are weak bases.

The prodcedure was the same as for alcohols. Perfectly satisfactory results were obtained in the case of the majority of the amines investigated (see Table 1).

In the case of α- and β-naphthylamines the sample was dissolved in a small amount of diethyl ether, and the dioxane-sulfotrioxide solution was added to the ether solution under cooling with snow. In this manner it was possible to avoid ring sulfonation, although with β-naphthylamine this reaction does nevertheless proceed to a certain extent, so that the results are a little high. The presence of ether did not alter the titer of the reagent. In the case of diphenylamine, not even cooling led to the desired results, and determination gave 1.54 active hydrogens in the molecule instead of 1. Due to the facility with which the resultant sulfamic acids are hydrolyzed, it is evidently impossible to determines amines with strongly negative substituents. Thus, only 0.52 active hydrogen is determined in p-nitroaniline, and 0.69 in o-nitrotoluidine. A very low result was also obtained with 2,4-dichloroaniline which only titrates to the extent of 10%.

We exploited the possibilty of determination of aromatic amines with the help of dioxane-sulfotrioxide for development of a new method of determination of aromatic aldehydes. The basis of the method is the reaction of aniline with aromatic aldehydes with formation of anils and water:

$$C_6H_5NH_2 + ArCHO \rightarrow ArCH{=}NAr + H_2O.$$

The reaction goes quickly and quantitatively even at room temperature. The aniline is taken in excess over the weighed sample of aldehyde. Unreacted aniline is determined with the help of dioxane-sulfotrioxide. It was established in preliminary experiments that anils do not react with the sulfur trioxide solution under the conditions of analysis.

TABLE 1

Amine	Percent active hydrogen		Number of active hydrogens in molecule
	calculated	found	
Aniline	1.08	1.09	1.01
o-Toluidine	0.94	0.93	0.99
p-Toluidine	0.94	0.95	1.01
m-Toluidine	0.94	0.97	1.04
Xylidine	0.83	0.86	1.04
p-Anisidine	0.81	0.81	1.00
α-Naphthylamine	0.70	0.70	1.00
β-Naphthylamine	0.70	0.77	1.10
Benzidine	1.09	1.08	1.99
Methylaniline	0.94	0.91	0.97
Ethylaniline	0.83	0.86	1.04

Method of determination

A solution of dioxane-sulfotrioxide was prepared by the usual method by passage of a mixture of air and sulfuric anhydride into dioxane. The weighed samples of aldehyde and aniline were taken in a small beaker, 5-7 mm high, with an internal diameter of 10-12 mm. The beaker with the samples was placed in a 50-ml conical flask by means of tweezers. The formation of anilines was complete within 15-20 minutes. After this, a measured volume of dioxane-sulfotrioxide solution was run into the flask from a piper with two marks making sure meanwhile that the beaker fills with dioxane solution. After 3-5 minutes, about 10 ml water was added, then indicator and the solution was rapidly titrated with 0.1 N soda solution. The indicator was either the usual solution of Congo red or bromophenol blue. A blank experiment was run in parallel with the experiment; titration of a fixed volume of sulfuric anhydride after diluting it with water. Each determination took 24-30 minutes.

It was readily apparent that the amine reacted in equivalent quantities with both the aldehyde and with dioxane-sulfotrioxide and, therefore, calculation was by the formulas:

$$\% \text{ CHO-group} = \frac{(b + d) \cdot N \cdot 29}{S \cdot 10} \; ; \; c = \frac{Sa \cdot 1000}{Ma} \, ,$$

$$\text{Number of CHO-groups} = \frac{\%CHO \cdot M}{100 \cdot 29} \, ,$$

where a is the number of milliliters of 0.1 N soda solution necessary to titrate the blank experiment; b is the number of milliliters of 0.1 N soda solution necessary to titrate after reaction with the weighed sample; c is the number of milliliters of 0.1 N soda solution (calculated), spent on a weighed sample of aniline; d = a − c is the decrease in the number of milliliters of 0.1 N soda solution (in comparison to the blank experiment); Sa is the weight of the sample of aniline (in g); Ma is the molecular weight of aniline; N is the normality of the soda solution; M is the molecular weight of the substance; S is the weight of the sample of investigated substance (in g).

Table 2 gives the results on the determination of the carbonyl group in the aromatic aldehydes. The samples of aldehydes were taken in weights 0.01-0.025 g and correspondingly for aniline 0.02-0.04 g. Two-fold increase of the sample weights (0.05-0.06 g for aldehyde and 0.11-0.12 for aniline) gave the same results but the accuracy of the determination was somewhat higher due to the increased difference in the volume of soda spent on the blank experiment and on the titration of the weighed sample.

The anils of certain aldehydes were yellow; this color became more intense later upon addition of dioxane-sulfotrioxide; therefore, the titration of cinnamaldehyde and nitrobenzaldehydes on Congo was carried out not until pink, but until the color of the indicator was orange-yellow; the color of bromophenol blue for these aldehydes changes to green and not to blue.

Our attempts to carry out the determination for aliphatic aldehydes did not yield the desired results, possibly since, as is known from the literature data [3], the reaction of the formation of anils with aliphatic aldehydes does not go analogously.

Under the conditions of aldehyde determination, the ketones reacted very incompletely with aniline, which makes the determination of aldehydes in presence of ketones unfeasible.

TABLE 2

Investigated substance	% CHO		Number of CHO-groups in molecule
	calculated	found	
Benzaldehyde	27.36	28.3	1.03
p-Methoxybenzaldehyde	21.3	20.9	0.98
Cinnamaldehyde	21.9	22.2	1.01
p-Nitrobenzaldehyde	19.2	19.1	0.99
m-Nitrobenzaldehyde	19.2	20.6	1.06
o-Nitrobenzaldehyde	19.2	19.0	0.98
Piperonal	19.33	19.3	0.99
p-Chlorobenzaldehyde	20.7	20.4	0.98
p-Dimethylaminobenzaldehyde	19.46	19.4	0.99
Cumaldehyde	19.6	19.4	0.99

SUMMARY

1. The possibility of utilizing a solution of sulfur trioxide in dioxane for quantitative determination of amino groups in aromatic amines is demostrated.

2. Aromatic amines containing negative substituents cannot be determined by this method.

3. A method was developed for quantitative determination of aromatic aldehydes with the help of dioxane-sulfotrioxide. The mean accuracy of the method is ± 3-5 %.

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HYDROXYDIHYDROFURANS

IV. THE PROBLEM OF THE BASIC PROPERTIES OF SUBSTITUTED 2-HYDROXYDIHYDROFURANS-2,5

E. D. Venus-Danilova and A. Fabritsy

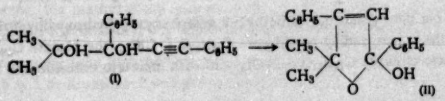
The first representative of the substituted hydroxydihydrofurans – 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 (II) – was obtained in 1915 from unsymm. dimethyl-phenyl-phenylethynyl-ethylene glycol (2-methyl-3,5-diphenylpentyn-4-diol-2,3) (I) by heating with 30% sulfuric acid [1].

The prepared substance possessed marked basic properties and formed with acids colored simple and complex salts which fluoresced in solutions. All these salts contained 1 mole of the substance to 2 moles of acid.

The structure of an alcohol-oxide (XVI) was attributed to the compound with basic properties. Salt formation was explained by the ability of the prepared substance to form oxonium compounds, and it was assumed that one molecule of acid was linked to the oxide oxygen and the other to the hydroxyl oxygen.

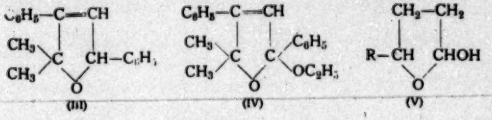
Later investigations of E. D. Venus-Danilova and co-workers [2-10], whose aim was the clarification of the influence of various radicals of ditertiary α-glycols of the acetylenic series upon the course of their rearrangements and also the study of some properties of the hydroxydihydrofurans prepared in the course of the work [11-14], enabled the compounds with basic properties to be assigned the structure of 2-hydroxydihydrofurans-2,5 (II) [11]. It was also shown that the mass of experimental data could not be reconciled with basic properties of the oxygen, i.e. its ability to form oxonium compounds [15-18]. As far back as the start of the 20th century Decker and Fellenberg [19] had noted the contradictions in theories of the structure of oxonium compounds in connection with the discovery of carbonium compounds.

We set out to clarify, if possible, the problem of the structure of salts of 2-hydroxydihydrofurans-2,5 with reference to the most closely studied compound – 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 (II):



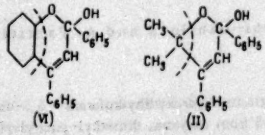
(I) (II)

The following characteristics suggest that 2-hydroxydihydrofuran-2,5 is a carbonium base similar to flavenol, benzpyranol and xanthydrol: the great mobility of the hydroxyl group of 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 which is manifested in its reduction [12] since the hydroxyl is first replaced by hydrogen and then the double bond is hydrogenated (III); the extraordinary ease of formation of ethers of 2-hydroxydihydrofurans [11, 3, 4] (IV) by reaction with alcohols; the reaction of their perchlorates with organomagnesium compounds with formation of dihydrofurans-2,5 (XXII); the absence of basic properties from 2-hydroxytetrahydrofurans (V) [20] and from 5,5-dimethyl-4,5-diphenyldihydrofuran-2,5 (III) [12]; and the formation of colored simple and complex salts [1, 3, 4]. In analogy with benzopyrilium salts, the salts of 2-hydroxydihydrofuran-2,5 may be called dihydrofurylium salts.



(III) (IV) (V)

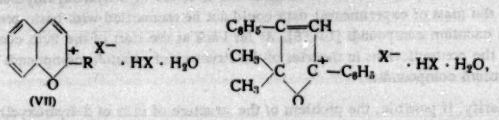
A similarity may be observed between the structural formulas of 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 (II) and, for example, 4-phenyl-flavenol-2 (VI):



(VI) (II)

A similarity can also be observed between the properties of flavilium, pyrilium and xanthilium salts on the one hand and those of dihydrofuryliumsalts on the other. Thus, for instance, the literature describes a series of colored simple and complexsalts of substituted xanthenols [21] as well as benzo- and naphthopyrilium salts [19, 22]; the composition of some of these salts may be represented by the formula: compound · 2HX. When crystallized from an aqueous solution of acid, the salts contain water of crystallization [21,22]. Complex salts containing platinum, gold and tin have the composition: 2 compound · $2HCl \cdot PtCl_4$; compound · $HCl \cdot AuCl_3$ [21-23].

Previously described salts of hydroxydihydrofuran [1] have an entirely different composition. Assuming that a carbonium ion is present in dihydrofurylium salts, their structure may, by analogy with the structure of benzopyrilium salts (VII), be represented by the following structural formulas:



(VII)

or $(C_{19}H_{17}O)Cl \cdot HCl \cdot H_2O$, $(C_{19}H_{17}O)AuCl_4 \cdot H_2O$, $(C_{19}H_{17}O)SnCl_5 \cdot H_2O$, $(C_{19}H_{17}O)_2PtCl_6 \cdot 2H_2O$.

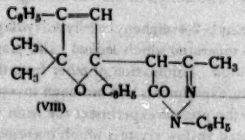
For confirmation of our theory that 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 is a carbonium base, we also synthesized the corresponding perchlorate $C_{19}H_{17}O \cdot ClO_4$, the picrate $C_{19}H_{17}O \cdot OC_6H_2(NO_2)_3$, and complex salts with ferric chloride $C_{19}H_{17}O \cdot FeCl_4$, and with mercuric chloride and bromide $C_{19}H_{17}O \cdot HgX_3 \cdot H_2O$.

We limited ourselves to the perchlorate, picrate and the complex salt with ferric chloride because the corresponding benzopyrilium, xanthilium, etc. salts nearly always have the composition (compound - HO)·X [21-26]. It was found that the salts which we synthesized, with exception of the mercury salt, likewise did not contain water of crystallization. This is further confirmation of our theory that we were dealing not with oxonium but with carbonium salts.

We also studied the reaction of 5,5-diemthyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 with phenylmethylpyrazolone and the reaction of the perchlorate of the same compound with methyl magnesium iodide.

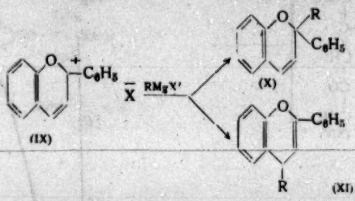
Bearing in mind that the carbinol compounds obtained on hydrolysis of triphenylmethane dyes contain an extremely mobile hydroxyl group and are capable of condensation with substances containing labile hydrogen atoms (aldehydes of the aliphatic series, nitromethane [27] or 1-phenyl-3-methyl-pyrazolone-5 [28]), we carried out the condensation of 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 with phenylmethylpyrazolone by the method of O. F. Ginzburg and V. R. Terushkin [28]. The result of the rapid reaction was formation of

the condensation product (VIII).



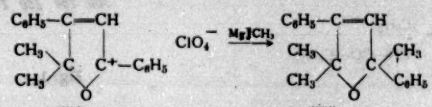
(VIII)

We also know from the literature that flavilium salts (IX) react with facility with organomagnesium compounds with formation, on addition of a radical in the 2-position of the pyran ring, of substituted α-chromenes (X), while addition in the 4-position gives γ-chromenes (XI) [29]. The direction taken by the reaction is governed by the position of the substituents in the pyran ring; for example, salts of flavilium chloride give γ-chromenes, but if the 4-position is occupied by a substituent (4-phenylflavinium chloride) then α-chromenes are formed:



(IX) (X) (XI)

Reaction of the perchlorate of 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 (XII) with methyl magnesium iodide gave a quantitative yield of 2,5,5-trimethyl-2,4-diphenyldihydrofuran-2,5 (XIII):



(XII) (XIII)

As has been expected, the methyl group adds on in the 2-position, since a phenyl group occupies the 4-position of the perchlorate of 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5.

It has already been pointed out that the first product of hydrogenation of 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 is 5,5-dimethyl-2,4-diphenyldihydrofuran-2,5 (III) which is later reduced to 5,5-dimethyl-2,4-diphenyltetrahydrofuran. This is a further illustraion of the resemblance to flavilium salts, which on catalytic reduction in presence of colloidal palladium or platinum at first are transformed into α-chromenes and subsequently into chromans [30-32].

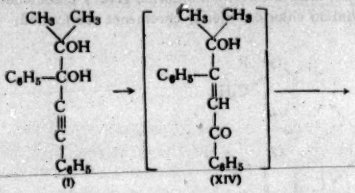
All compounds that form the carbonium ion give ethers very readily on reaction with alcohols in presence of a few drops of concentrated acetic acid [19, 33-35]. We previously described similar ethers of the type of full kerals (IV) for three substituted 2-hydroxydihydrofurans-2,5 [11,3,4].

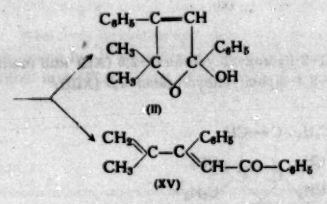
The basic properties of 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 are confirmed by our determinations of its hydrolysis constant (of the order of $1.2 \cdot 10^{-5}$) by potentiometric titration in 60% acetone.

In Figs. 1, 2 and 3 are plotted the absorption spectra in the ultraviolet and in the long-wave portion of the spectrum for 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 ($C_{18}H_{18}O_3$; $\lambda_{max.}$ 252 mμ, ε 7304.6) (Fig. 1), its hydrochloride ($C_{18}H_{17}OCl \cdot HCl \cdot H_2O$; λ_{max} 252mμ, ε 18145.4; λ_{max} 308mμ, ε 121.3; λ_{max} 400mμ, ε 565.9) (Fig. 2) and hydrobromide ($C_{18}H_{17}OBr \cdot HBr \cdot H_2O$; λ_{max} 248mμ, ε 16027.3; λ_{max} 308—308mμ, ε 100.2;

λ_{max} 400mμ, ε 502.9) (Fig. 3) in alcoholic solutions.* The spectra are identical except for the fact that hydrofurylium salts, in contrast to the base, also absorb in the visible region of the spectrum.

In the preparation of 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 by the usual method [1], yet another product of reaction could be separated which lacked basic properties and could therefore be easily extracted with ether from the acid solution. Elimination of ether from this extract usually left a small amount of a viscous resin which in the preceding experiments had not been investigated due to the high yields of 2-hydroxydihydrofuran-2,5 (about 70 %). In the present experiment the resin was retained and after a few months it deposited a small quantity of well-formed yellow crystals which corresponded in structure to a dienic ketone — 2-methyl-3,5-diphenyl-pentadiene-1,3-one-5 (XV). This ketone may have been formed by dehydration of the unsaturated olefinic γ-ketoalcohol (XIV), which was not separated in the isomerization of dimethyl-phenyl-phenylethynyl-ethylene glycol (I). The corresponding γ-ketoalcohols or products of their decomposition were detected in transformations of some other α-glycols of the acetylenic series [3, 6-9].





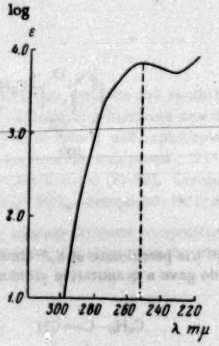


Fig. 1.

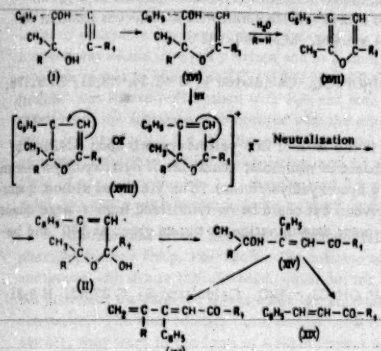
One of us [11] had earlier put forward such a scheme for transformation of α-glycols.

Transformations of acetylenic α-glycols in an acid medium can, however, be condisdered from a somewhat different angle if we assume the primary product of transformation to be not the olefinic γ-ketoalcohol (XIV) but the dihydrofurylium salt (XVIII).

It may be suggested, as was assumed earlier [1] and as was not excluded (as possible variant) by L. A. Pavlova [36], that the first stage of transformation of the pinacone (I) is its cyclization with formation of a substituted 4-hydroxydihydrofuran-4,5 (XVI). If the 5-position in 4-hydroxydihydrofuran-4,5 is occupied by a hydrogen atom, a molecule of water splits off and the substituted furan (XVII) is obtained. But if removal of water is impossible, a dihydrofurylium salt (XVIII) is formed and partial hydrolysis of the latter gives the substituted 2-hydroxydihydrofuran-2,5. Transformation of 4-hydroxydihydrofuran-4,5 (XVI) into 2-hydroxydihydrofuran-2,5 (II) via the cation of salt (XVIII) finds confirmation in the fact that substituted 2- and 4-benzopyranols give one and the same salt, which on hydrolysis in presence of alcohol forms derivatives of substituted 2-benzopyranol [35, 43]. 2-Benzopyranols are generally more stable than 4-benzopyranols.

Subsequently 2-hydroxydihydrofuran may undergo ring fission to give the olefinic γ-ketoalcohol (XIV) and products of its further transformation (XV, XIX):

* Photometric measurements of the spectra were carried out on the SF-4 spectrophotometer of U. A. Dranitsina, for which we convey to her our thanks.



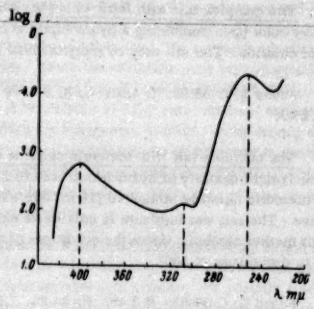


Fig. 2

The proposed scheme enables us to compare the formation of substituted 2-hydroxydihydrofurans-2,5 from ditertiary α-glycols of the acetylenic series with the preparation of substituted furans from secondary-tertiary [37] and primary-tertiary [36] α-glycols of this series.

So support for the proposed scheme may be said to be provided by the formation dimethylpyrone of the unsaturated diketone — 4-phenyl-hexen-3-dione-2,6- by the action of phenyl magnesium bromide and then of perchloric acid [38].

The author attributes the structure of a pyroxonium salt and not of a carbonium salt to the perchlorate of dimethyl-phenylpyrone, but this does not alter the development of the argument.

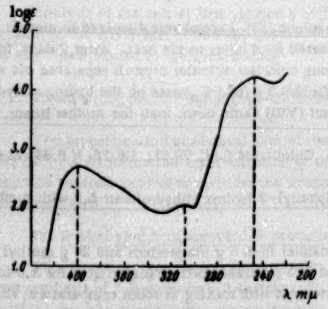


Fig. 3

EXPERIMENTAL

1. Preparation of simple and complex salts of 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5.

The perchlorate came down in almost quantitative yield upon running an etheral solution of perchloric acid into an ethereal solution of hydroxydihydrofuran. The solution of acid was run in until precipitate stopped coming down. The salt was obtained in the form of a lemon-yellow powder, insoluble in ether and benzene, difficultly soluble in alcohol; m.p. 203-204° (decomp.).

Found%: C 61.69; H 4.28; Cl 10.04, 10.31. $C_{18}H_{17}O \cdot ClO_4$. Calculated%: C 61.99; H 4.48; Cl 10.19.

The picrate separated out in the form of orange well-formed acicular crystals upon combining solutions of

0.3 g hydroxydihydrofuran in 5 ml alcohol and 0.3 g picric acid in 5 ml alcohol. M.p. 168-169°. It was quite readily soluble in alcohol.

Found %: C 60.22; H 4.29; N 8.99. $C_{18}H_{17}O \cdot OC_6H_2(NO_2)_3$. Calculated %: C 60.38; H 3.98; N8.81.

The complex salt with ferric chloride was obtained in the form of fine crystalline powder of a brown-yellow color upon combining a hydrochloric acid solution of hydroxydihydrofuran with an aqueous solution of ferric chloride. The salt may be recrystallized from methyl alcohol. M.p. 147-148°.

Found %: C 48.20; H 4.01; Cl 31.63; Fe 12.44. $C_{18}H_{17}OFeCl_4$. Calculated %: C 48.34; H3.81; Cl 31.78; Fe 12.49.

The complex salt with mercuric chloride came down in the form of fine yellow crystals upon addition of an equivalent quantity of hydrochloric acid (d 1.19) to a mixture of equimolar quantities of hydroxydihydrofuran and mercuric chloride in alcohol (10 ml 96% alcohol per 1 g hydroxydihydrofuran). The yield was almost quantitative. The salt was insoluble in cold water and organic solvents but could be recrystallized from a large quantity of methyl alcohol. Under the conditions of the melting-point determination, it turned green at 140° and began to decompose at 160°.

Found %: C 37.83; H 3.42; Hg 34.85; Cl 18.28. $C_{18}H_{17}OHgCl_3 \cdot H_2O$. Calculated %: C 37.63; H 3.31; Hg 34.96; Cl 18.55.

The complex salt with mercuric bromide was prepared similarly to the preceding salt by taking mercuric bromide and hydrobromic acid. In view of the fact that mercuric bromide is less soluble in alcohol than mercuric chloride, twice the amount of alcohol must be taken. Yield 81% (due to partial solubility in alcohol). Fine yellow crystals with an orange tinge (after recrystallization from methyl alcohol), decomposes at about 180-185° upon melting point determination.

Found %: Br 33.40, 33.38; Hg 28.41. $C_{18}H_{17}OHgBr_3 \cdot H_2O$. Calculated %: Br 33.92; Hg 28.35.

II.. Condensation of 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 with 1-phenyl-3-methylpyrazolone-5 (VIII).

0.3 g 2-hydroxydihydrofuran and 0.3 g phenylmethylpyrazolone (50% excess) were dissolved in methyl alcohol (15 ml for both substances); the solutions were combined and heated for 4 hours to the boil. After 2 days, from the slightly darkened liquid, upon standing in an open vessel, long colorless acicular crystals separated out which after being washed with methyl alcohol had m.p. 137-138°. Yield 0.3 g (63.5%, based on the hydroxydihydrofuran taken). A small additional amount of condensation product (VIII) came down from the mother liquor.

Found %: C 79.32; H 6.40; N 6.26. M 419. $C_{28}H_{26}O_2N_2$. Calculated %: C 79.61; H6.16; N 6.63. M 422.

III. Reaction of the perchlorate of 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 with methylmagnesium iodide.

To the methylmagnesium iodide, prepared in the usual manner from 5 g magnesium and 30 g methyl iodide in 150 ml absolute ether, 18 g dry perchlorate was added in 5 different portions (calculated for 3.5-fold excess of organomagnesium compound). The reaction was carried out with mixing at room temperature; slight evolution of heat was noted upon adding the perchlorate. After all the perchlorate had been added, the reaction mass was heated for 30 minutes to a weak boil of ether and, after cooling, was poured on ice, decomposed with ammonium chloride and extracted with ether. After drying with sodium sulfate and driving off the ether, the remaining colorless liquid had b.p. 163° upon vacuum distillation (2 mm).

The substance contained no hydroxyl group (negative reaction with methylmagnesium iodide), gave no fluorescence with strong sulfuric acid but gave a brown solution which formed an emulsion upon dilution with water; it reacted quite slowly with bromine in chloroform and with potassium permanganate.

Yield 10,5 g substance with a rather pleasant odor (78%, based on substance being 2,2,5-trimethyl-3,5-diphenyldihydrofuran-2,5).

B.p. 163° (2 mm), n_D^{20} 1.5736, d_4^{20} 1.0660, MR_D 81.67, $C_{19}H_{20}O$ F, calc. 81.72.

Found %: C 86.15, 86.01; H 7.92, 7.95. M 256. $C_{19}H_{20}O$. Calculated %: C 86.37; H 7.60. M 264.

Oxidation of substance with b.p. 163° (2 mm). For the oxidation we took 6 g of the substance and 12 g potassium permanganate (calculating 5 moles oxygen per 1 mole dihydrofuran). To 400 ml 1.5% aqueous solution of potassium permanganate in the cold was added all the oxidized substance. The remaing quantity of oxidant was added in small portions and in a finely divided state. Since the oxidation went very sluggishly, the reaction mass was heated at 45° for 6 hours. After this potassium permanganate color disappeared, manganese dioxide was filtered off, washed with H_2O, and then with ether. After addition of 0.3 g soda, ethereal extracts were taken from the filtrate and combined with the ether after washing the manganese dioxide. After driving off the ether, we obtained 2.5 g oily liquid with the odor of acetophenone. The content of acetophenone in the mixture of neutral oxidation products was determined via the 2,4-dinitrophenylhydrazone and corresponded to 40%. The yield of acetophenone was 1 g; the obtained 2,4-dinitrophenylhydrazone had m.p. 249-250° and gave no melting point depression with known 2,4-dinitrophenylhydrazone of acetophenone.

Acetone was driven off from the aqueous solution of organic acid salts and characterized by its 2,4-dinitrophenylhydrazone (m.p. 124-125°). The solution of organic acid salts was concentrated on a water bath and decomposed with dilute sulfuric acid. Upon boiling an aqueous solution with distillation of the volatile acids, in the distillate we detected traces of formic acid and a small amount of benzoic acid which separated out in the condenser. The non-volatile (with steam) acids (2 g) were obtained after ether was removed from their ethereal extract; they were in the form of a thick viscous mass from which, upon standing, crystals started to separate out. The crystals were purified on a porous plate and had m.p. 65-67°; they gave a melting point depression with benzoic acid. The acid was quite readily soluble in hot water, quite readily sublimed and had a pleasant honey-like odor. After sublimation, its melting point was unaltered.

Found number of active hydrogens: 1.93; % OH 20.44; equiv. 168. $C_9H_{10}O_3$. Calculated number of active hydrogens 2; % OH 20.48; equiv. 166.

A portion of the acid was converted via ammonium salt to the silver salt. It was washed with warm water (it wetted very poorly and was relatively readily soluble in hot water) and dried in a desiccator; the salt was stable on keeping and in solutions on heating.

Analysis of the salt at first yielded a high silver content (40.41% against 39.55), probably due to slight admixture of the silver salt of benzoic acid. After purification by fractional crystallization, the silver content of the salt corresponded to the theoretical.

Found %: Ag 39.33. $C_9H_9O_3Ag$. Calculated %: Ag 39.55

The properties and analytical data of the acid with m.p. 65-67° corresponded to methylphenylglycolic acid [39] but its formation upon oxidation of the substituted dihydrofuran together with benzoic acid, acetophenone and acetone lead us to consider the structure of the dihydrofuran to be 2,5,5-trimethyl-2,4-diphenyldihydrofuran-2,5 (XIII).

IV. 2-Methyl-3,5-diphenyl-1,3-pentadienone-5 (XV).

This diolefinic ketone was isolated from the resin obtained from the ethereal extract of the acid solution upon synthesis of 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 from an acetylenic pinacol — unsymmetrical dimethylphenyl-phenylacetylenylethylene glycol (I). Upon standing, crystals started to come down from the resin within 5-6 months. For isolation, the crystals with the resin were washed on a porous plate with gasoline (b.p. 85-110°). After recrystallization from boiling gasoline, we obtained well-formed, large, thick, bright-yellow needles with m.p. 92-93°.

The substance did not contain hydroxyl groups and rapidly decolorized a solution of potassium permanganate and a solution of bromine in chloroform, and with 2,4-dinitrophenylhydrazine gave a bright-red 2,4-dinitrophenylhydrazone with m.p. 155-156°.

Analysis of the substance with m.p. 92-93°. Found %: C 86.77, 86.87; H 6.84, 7.01. M 240.8 $C_{18}H_{16}O$. Calculated %: C 87.10; H 6.45. M 248.

Analysis of the 2,4-dinitrophenylhydrazone with m.p. 155-156°. Found %: C 67.05, H 5.02; N 13.47. $C_{24}H_{20}O_4N_4$. Calculated %: C 67.28; H 4.67; N 13.08.

Ozonation of the substance with m.p. 92-93° was carried out in chloroform. 1.006 g ozone was spent on 2 g of substance (130% calculated on diolefinic ketone). Yield 3.65 g solid yellow ozonide. After the usual decomposition of the ozonide and alkalization of the solution, the neutral products were extracted with ether. A small amount of viscous yellow liquid (about 0.3 g) with a peculiar pungent odor was isolated which came over with the steam; from it we prepared the bright-red p-nitrophenylhydrazone which was insoluble in ordinary solvents and decomposed at about 230-233°.

Upon standing, flakes separated out from the liquid which after purification on a porous plate melted at about 206-211°. Due to their small quantities the first and second substances were not investigated in greater detail but it may be assumed that the first was the diketone — acetylbenzoyl [40] and the second its condensation product — 2,5-diphenylquinone [41].

Acidification of the organic acid salts yielded 1.6 g benzoic acid with m.p. 118-119° (mixing test) and the sharp odor of the organic acids was perceived (probably of acetic and formic). After removal of benzoic acid, a qualitative reaction with phenylhydrazine hydrochloride [42] revealed a small amount of benzoyl formic acid in the solution and the presence of formic acid in the distilled aqueous solution was shown by reduction of mercuric chloride and an ammoniacal solution of silver oxide. The high content of benzoic acid may be due to the decomposition of not only benzoyl formic acid but also the partial oxidation of acetylbenzoyl.

The obtained ozonation products permit us to consider the diolefinic ketone to be 2-methyl-3,5-diphenylpentadien-1,3-one-5.

From 30 g glycol we obtained 2.9 g (10.4%) crude ketone and after two recrystallizations from the light gasoline fraction we obtained 2.5 g (9%).

SUMMARY

1. It is shown that the basic properties of 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 are governed by formation of the carbonium ion. This compound gives salts that are completely analogous to the benzopyrilium, flavinium and xanthilium salts, and they may be called dihydrofurylium salts.

2. A series of new ethers of salts of 2-hydroxydihydrofuran is obtained and confirms the structure of the salts of 2-hydroxydihydrofuran-2,5.

3. Condensation of 2-hydroxydihydrofuran with methylphenylpyrazolone is effected; this confirms the great mobility of the hydroxyl group of 2-hydroxydihydrofuran.

4. The reaction of an organomagnesium compound with dihydrofurylium perchlorate is studied.

5. A dienic ketone — 2-methyl-3,5-diphenyl-pentadien-1,3-one-5 — is isolated from the products of isomerization of unsymm. dimethyl-phenyl-phenylethynyl-ethylene glycol in an acid medium.

6. A mechanism for the formation of 5,5-dimethyl-2,4-diphenyl-2-hydroxydihydrofuran-2,5 under the influence of sulfuric acid is proposed.

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REACTION OF m-NITROPHENOL WITH SYMMETRICAL MERCURY COMPOUNDS

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It was established in a series of researches [1-3] that reaction of aromatic compounds of mercury with phenols takes place with formation of mercurated compounds of phenol. The reaction proceeds according to the following equation:

$$ArHgAr \rightarrow [ArHg^{\cdot} + Ar^{\cdot}] + C_6H_4(OH)(R) \rightarrow C_6H_3(OH)(R)HgAr + ArH.$$

Mercurated derivatives of phenols are crystalline compounds which decompose on heating with separation of free metallic mercury. Their susceptibility to decomposition (in other words, their thermal stability) is governed to a considerable extent by the nature of the substituents in the phenol ring.

It was found that in the case of various first order substituents, the compounds obtained were less stable than in the case of second order substituents. The position of the substituting groups in the phenolic ring at the same time influences the thermal stability [4]. In the case of nitrophenols the most stable mercurated compounds are derivatives of o-nitrophenol, while the least stable are the derivatives of m-nitrophenol.

The present investigation relates to the mercuration of derivatives of m-nitrophenol. In respect of thermal stability the prepared compounds stand, so to speak, at the boundary between the unstable compounds of phenols containing first order substituents and the extremely stable p- and o-nitrophenols.

We studied the reaction of m-nitrophenol with di-p-aminophenyl-mercury, ditolyl-mercury, dimethoxyphenyl-mercury, and biphenyl-mercury. The reaction was carried out in sealed ampoules at 70, 100, 130 and 150° and with various durations of heating (3-6 hours).

The investigations showed that reaction of the above-noted symmetrical aromatic compounds of mercury with m-nitrophenol goes with formation of two kinds of products. On the one hand we obtained 4 monomercurated derivatives of m-nitrophenol which differed from one another in respect of the radical attached to the mercury:

(I) $m\text{-}C_6H_3(OH)(NO_2)HgC_6H_5$

(II) $m\text{-}C_6H_3(OH)(NO_2)HgC_6H_4CH_3\text{-}p$

(III) $m\text{-}C_6H_3(OH)(NO_2)HgC_6H_4NO_2\text{-}p$

(IV) $m\text{-}C_6H_3(OH)(NO_2)HgC_6H_4OCH_3\text{-}p$

On the other hand, in all the experiments one more compound was obtained whose composition and properties did not alter with the nature of the symmetrical compound of mercury taken in the reaction. This substance contained mercury and free hydroxyl groups. On the basis of analyses we assigned to it the formula of di-(m-hydroxynitrophenyl)-mercury:

$$m\text{-}(O_2N)(OH)C_6H_3HgC_6H_3(OH)(NO_2)$$

This compound is formed as a result of breakdown of the primarily formed mercurated derivatives of m-nitrophenol ($RArC_6H_4)_2Hg$ into radicals and their subsequent interaction with a fresh molecule of m-nitrophenol:

$$RArHgC_6H_3(OH)(NO_2) \rightarrow [RAr^{\cdot} + {}^{\cdot}HgC_6H_3(OH)(NO_2)] + C_6H_4(OH)(NO_2) \rightarrow (O_2N)(OH)C_6H_3HgC_6H_3(OH)(NO_2) + RArH.$$

For confirmation of this hypothesis we reacted one of our synthesized mercurated derivatives of m-nitrophenol with m-nitrophenol.. As a result we actually obtained di-(m-hydroxynitrophenyl)-mercury and aniline:

$$H_2NC_6H_4HgC_6H_3(OH)(NO_2) + C_6H_4(OH)(NO_2) \longrightarrow$$

$$\longrightarrow (O_2N)(OH)C_6H_3HgC_6H_3(OH)(NO_2) + C_6H_5NH_2$$

EXPERIMENTAL

Reaction of m-nitrophenol with di-p-aminophenylmercury. The reaction was carried out at different temperatures; 70, 100, 130, 150°. Heating lasted 3 hours. At one temperature (130°) an experiment was performed with heating for 6 hours.

In all experiments the starting substances were taken in identical quantities by weight.from 0.2 to 0.4 g. The reaction was carried out in sealed ampoules.

Separation of the substances after opening the ampoules was effected quite readily due to their different solubilities. As example we present one typical experiment.

Heating for 3 hours at 100°. After the ampoules were opened, aniline was removed from the reaction mass and identified via the benzoyl derivative. The residue was treated with aqueous alcohol to remove the unreacted m-nitrophenol. The insoluble mass was treated with heated alcohol from which, upon cooling, green crystals of $(NO_2)(OH)C_6H_3HgC_6H_4(NO_2)$ came down; weight 0.120 g. For purification, the substance was dissolved in 2 N KOH and precipitated by gaseous CO_2. Yellow crystals were obtained with m.p. 225° (with decomp.).

Found %: Hg 45.63. $C_{12}H_{10}O_5N_2Hg$. Calculated %: Hg 42.58.

The alcohol-insoluble residue was in the form of fluffy yellow-green crystals with m.p. 244-245° (with decomp.), and was $(NO_2C_6H_3OH)_2Hg$. Yield 0.45 g.

Found %: Hg 42.68 $C_{12}H_8O_6N_2Hg$. Calculated %: Hg 42.08.

At 130 and 150° metallic mercury formed due to decomposition of the starting and formed substances. The mercury was analyzed by the usual method.

The data for all the experiments that were carried out are given in Table 1.

Confirmation of the structure $(NO_2)(OH)C_6H_3HgC_6H_4(NH_2)$. For the experiment the substance was taken in the form of yellow scalelike crystals with m.p. 224-225° (with decomp.).

The ability of the given compound to dissolve in alkali and be precipitated out by CO_2 indicates the presence of free phenolic hydroxyl.

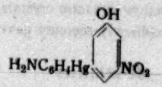
TABLE 1

Reaction and decomposition products	70° 3 hours	100° 3 hours	130° 3 hours	130° 6 hours	150° 3 hours
$(NO_2)(OH)C_6H_3HgC_6H_4(NH_2)$ (in g)	0.380	0.120	0.168	–	–
$[(NO_2)(OH)C_6H_3]_2Hg$ (in g)	–	0.450	0.240	0.156	–
Hg (in %)	–	—	6.86	15.28	81.17

Alcoholic HCl solution brought about cleavage of the substance and formation of white crystalline p-aminophenylmercury chloride with m.p. 200°, identified by mixing test. m-Nitrophenol with m.p. 96° was isolated from the ethereal extract. A mixed sample gave no depression.

The position of the mercury atom in the nitrophenol ring was determined by cleavage of the compound with bromine in aqueous solution of potassium bromide. In this case the mercury is replaced by bromine. This reaction yielded a crystalline substance with m.p. 139-140°. After recrystallization from petroleum ether, it was

in the form of fine lustrous crystals with m.p. 142-143°. This conincides with the literature data on the melting point of 3-nitro-5-bromophenol (143-145°) [4]. On the basis of this we believe we obtained 3-nitro-5-aminophenylmercury-1-hydroxybenzene (V).



(V)

Reaction of m-nitrophenol with di-p-methoxyphenylmercury. The reaction was carried out as in the preceding case at different temperatures (70,100,130,150°). Heating was continued for 3 hours. In all experiments the starting substances were taken in the same quantities by weight (0.20 g). As an example we present one typical experiment.

Heating for 3 hours at 70°. After the ampoules were opened, anisole was separated from the crystalline mass by means of a capillary pipet. M.p. 154° (Sivolob). To remove the unreacted nitrophenol the reaction mass was treated with aqueous alcohol. After two recrystallizations, from the insoluble precipitate we obtained pale-yellow crystals, weight 0.160 g with m.p. 230-232°.

Found %: Hg 44.22. $C_{19}H_{11}O_4NHg$. Calculated %: Hg 44.99.

TABLE 2

Reaction and decomposition products	70° 3 hours	100° 3 hours	130° 3 hours	150° 3 hours
$(NO_2)(OH)C_6H_3HgC_6H_4(OCH_3)$ (in g)	0.160	0.120	0.086	0.060
$[(NO_2)(OH)C_6H_3]_2Hg$ (in g)	–	–	0.250	0.160
Hg (in %)	–	–	–	5.28

The experimental data are given in Table 2.

Reaction of m-nitrophenol with o-ditolylmercury. The starting substances for the reaction were taken in 0.50 g samples. Heating was for 3 hours at 130°. After the ampoules were opened, toluene was driven off and m-nitrophenol was extracted with aqueous alcohol. The insoluble precipitate was bis-m-nitrophenylmercury in the form of soft yellow crystals with m.p. 246° (with decomp.). Yield 0.3860 g.

Reaction of m-nitrophenol with diphenylmercury. For the reaction we took 0.50 g samples of starting substances. The reaction was carried out with heating to 130° for 3 hours. After the ampoules were opened, first benzene was driven off. From the alcoholic extract we obtained a reaction product in the form of yellow crystals with m.p. 150° (with decomp.), weight 0.130 g.

Found %: Hg 47.70. $C_{12}H_9O_3NHg$. Calculated %: Hg 48.26.

The insoluble residue of di-(m-hydroxynitrophenyl) mercury was in the form of soft yellow crystals with m.p. 246° (with decomp.). Yield 0.65 g.

Confirmation of the structure of di-(m-hydroxynitrophenyl)-mercury m-$[NO_2(OH)C_6H_3]_2Hg$. 1.5 g substance was obtained in the form of soft yellow-green crystals with m.p. 245-246° (with decomp.) and a mercury content of 42.25 and 42.88%.

To confirm the presence of hydroxy groups in the compound the substance was dissolved in 0.5 N KOH. The substance was precipitated from the bright-red solution by carbon dioxide in the form of yellow-greenish soft crystals with m.p. 246° (decomp.). A mixed sample gave no depression.

The content of active hydrogen was also determined by the Chugaev transformation method.

Found: active H atoms 2.03, 2.08, 2.02. $[NO_2(OH)C_6H_3]_2Hg$. Calculated: active H atoms 2.

Confirmation of the formation of di-(m-hydroxynitrophenyl)-mercury. 0.10 g m-$(NO_2)(OH)C_6H_3HgC_6H_4NH_2$-p and 0.0500 g m-nitrophenol were heated in a sealed ampoule for 3 hours at 130°. When the ampoule was opened, aniline was detected (by isocyanide reaction). After treatment of the reaction mixture with alcohol, an insoluble precipitate remained in the form of yellow-greenish crystals, weight 0.0586 g, m.p. 246° (with decomp.). A mixed sample with known di-(m-hydroxynitrophenyl)-mercury gave no depression.

SUMMARY

1. The reaction of m-nitrophenol with diphenyl-mercury, with di-p-amino-phenyl-mercury, with di-p-methoxyphenyl-mercury and with di-o-tolyl-mercury was studied.

2. It was shown that in all cases monomercurated derivatives of m-nitrophenol are formed.

3. It was found that, apart from monomercurated derivatives of m-nitrophenol, di-(hydroxynitrophenyl)-mercury is obtained; the latter is formed as a result of reaction of the mercurated derivatives of m-nitrophenol with m-nitrophenol.

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SYNTHESES IN THE SERIES OF AROMATIC DERIVATIVES OF THIOUREA

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In recent years reports have appeared in the literature of the antitubercular activity, both in vitro and in vivo, of some derivatives of thiourea [1, 2, 3].

Studies were mainly made of N,N'-diaryl-substituted thioureas (thiocarbanilides) with various substituents in the benzene ring. The most interesting representatives of this series of compounds proved to be: 4,4'-di-alkyl- and dialkoxy-thiocarbanilides, in particular 4,4'-diethoxythiocarbanilide.

Derivatives of thiourea containing an aroyl residue at one or both nitrogen atoms have been rather neglected from the chemical angle, while they have not been investigated at all biologically. For this reason it appeared of interest to synthesize a series of N-aryl-N'-aroyl-substituted thioureas and to subject them to chemotherapeutic tests.

Compounds of this type were synthesized, starting from the chlorides of the corresponding acids, via the isothiocyanates according to the following scheme [10]:

$$RCOOH \xrightarrow{SOCl_2} RCOCl \xrightarrow{Pb(CNS)_2} RCONCS \xrightarrow{R'NH_2} RCONHCSNHR'$$

R' = p-tolyl, p-ethoxyphenyl, p-nitrophenyl;

R = phenyl, p-nitrophenyl, p-dimethylaminophenyl

The synthesis may be carried out both with separation of the intermediate isothiocyanates and without their separation; in the latter case the yield is considerably increased; thus, for N-p-nitrobenzoyl-N'-p-ethoxyphenylthiourea the yield is 90% reckoned on the p-nitrobenzoic acid. Some isothiocyanates were unstable substances and they could not be isolated in a sufficiently pure state (an example is p-dimethylaminobenzoyl isothiocyanate).

Thiourea derivatives containing a nitro group in the benzene ring were subjected to catalytic hydrogenation in presence of excess of skeletal nickel catalyst. In this way we obtained the corresponding amines, whose acetylation under mild conditions led to the acetyl derivatives. All the prepared compounds were handed over for chemotherapeutic tests.

For comparison of the activity of the prepared compounds with that of derivatives of thiocarbanilide, we synthesized 4,4'-diethoxythiocarbanilide. This compound had previously been obtained by reaction of p-phenetidine with carbon bisulfide in presence of hydrogen peroxide [4] or sulfur [5], and also by reaction of thiophosgene with p-phenetidine [6].

In view of the undesirability of working with carbon bisulfide in the preparation of large quantities of compounds, we tried to use the method of condensation of thiourea with amines for the synthesis of 4,4'-diethoxythiocarbanilide.

As we know from the literature, heating of thiourea with aniline [7,8] or with p-aminoacetanilide [9] gives, apart from monosubstituted thioureas, N,N'-disubstituted derivatives, although in very poor yield. We showed that by conducting the reaction with equimolar amounts of thiourea and p-phenetidine at 140°, a yield of ~30% of p-ethoxyphenylthiourea is obtained. Applying more drastic conditions (180-210°) with excess

of p-phenetidine, a yield of about 45% of 4,4'-diethoxythiocarbanilide is obtained, calculated on the reacted p-phenetidine.*

EXPERIMENTAL

N-Benzoyl-N'-p-ethoxyphenylthiourea. To a boiling solution of 5.9 g freshly-distilled p-phenetidine in 25 ml anhydrous benzene was added with stirring in the course of 20 minutes 7 g benzoyl isothiocyanate in 25 ml anhydrous benzene [11], and then the reaction mass was heated for 15 minutes more. Upon cooling, the precipitate which separated out was filtered off and carefully washed with benzene. The yield of N-benzoyl-N'-ethoxyphenylthiourea was 11.4 g (89%). Colorless needles with m.p. 146-148°, readily soluble in acetone, chloroform, ethyl acetate, dioxane, more difficultly soluble in alcohol, ether and insoluble in water. After two recrystallizations from alcohol, it had m.p. 147-148°.

Found %: C 63.48; H 5.33; N 9.35. $C_{16}H_{16}O_2N_2S$. Calculated %: C 63.93; H 5.33; N 9.33.

N-p-Acetaminobenzoyl-N'-p-ethoxyphenylthiourea. a) p-Nitrobenzoyl isothiocyanate. To a boiling suspension of 74 g p-nitrobenzoic acid in 300 ml anhydrous benzene with stirring we added 60 ml thionyl chloride drop-wise in the course of 30 minutes. The reaction mass was then boiled for 21 hours until complete solution of p-nitrobenzoic acid. After removal of the excess thionyl chloride and the benzene in vacuum, the residue (p-nitrobenzoyl chloride) was dissolved in 350 ml anhydrous benzene and the resulting solution with stirring was added drop-wise in the course of 1.5 hours to a suspension of 94 g lead thiocyanate in 100 ml boiling anhydrous benzene. When the reaction was complete, the precipitate was filtered off and the filtrate was evaporated down in vacuum; the residue was p-nitrobenzoyl isothiocyanate in the form of yellow needles with m.p. 78-83°. Weight 88.6 g. For purification a portion of the substance was vacuum distilled. p-Nitrobenzoyl isothiocyanate had b.p. 187-188° at 10 mm; m.p. 90-92°.

Found %: N 13.55. $C_8H_4O_3N_2S$. Calculated %: N 13.46.

b) N-p-Nitrobenzoyl-N'-p-ethoxyphenylthiourea. To a boiling solution of 33.4 g freshly-distilled p-phentidine in 50 ml anhydrous benzene with stirring was added drop-wise in the course of 50 minutes a solution of 50.5 g p-nitrobenzoyl-isothiocyanate in 250 ml anhydrous benzene and then the reaction mass was heated for 1.5 hours more. Upon cooling, the precipitate which separated out was filtered off and washed with benzene.

The yield of N-p-nitrobenzoyl-N'-p-ethoxyphenylthiourea was 74.4 g (88.7%) – orange needles, soluble in acetone, dichloroethane, ethyl acetate, dioxane, sparingly soluble in alcohol and ether. After two recrystallizations from benzene, it had m.p. 167-168.5°.

Found %: C 55.67; H 4.43; N 11.87. $C_{16}H_{15}O_4N_3S$. Calculated %: C 55.62; H 4.38; N 12.16.

c) N-p-Aminobenzoyl-N'-p-ethoxyphenylthiourea. To a suspension of 25 g commercial N-p-nitrobenzoyl-N'-p-ethoxyphenylthiourea with m.p. 156-163° in 450 ml ethyl acetate was added 12 g skeletal nickel catalyst (slurry) in alcohol. Hydrogenation was carried out at room temperature and atmospheric pressure for 11 hours.

The reaction mass was filtered free of catalyst, the ethyl acetate was driven off in vacuum; the residue (22.5 g) was recrystallized from alcohol. Yield 16.5 g slightly yellowish crystalline substance with m.p. 182-183°, soluble in ethyl acetate, acetone, chloroform, difficultly soluble in alcohol, insoluble in water.

Found %: C 61.19; H 5.56; N 12.59. $C_{16}H_{17}O_3N_3S$. Calculated %: C 60.92; H 5.45; N 13.32.

d) N-p-Acetaminobenzoyl-N'-p-ethoxyphenylthiourea. To a suspension of 3 g N-p-aminobenzoyl-N'-p-ethoxyphenylthiourea in 40 ml dry chloroform was added with stirring at room temperature 7.5 ml acetic anhydride. The reaction mass was boiled on a water bath. Soon all the substance dissolved and then a precipitate again came down. After further heating for 15 minutes the mixture was cooled, the precipitate was filtered off, washed with a small amount of cooled chloroform and dried in a vacuum desiccator. Yield 2.95 g white crystalline substance, soluble in ethyl acetate, more difficultly soluble in chloroform and alcohol, m.p. 190-190.5°.

Found %: C 60.28; H 5.38; N 11.28. $C_{18}H_{18}N_3O_3S$. Calculated %: C 60.6; H 5.33; N 11.76.

*The authors convey their deep gratitude to Prof. M. N. Shchukina for her interest in the present investigation.

N-p-Dimethylaminobenzoyl-N'-p-ethoxyphenylthiourea. To a boiling suspension of 9.2 g p-dimethylaminobenzoic acid (m.p. 238-239°) in 200 ml anhydrous benzene with stirring was added drop-wise 8 ml thionyl chloride. The reaction mass was then heated for 5 hours until complete solution of p-dimethylaminobenzoic acid.

After removing the excess thionyl chloride and the benzene in vacuum, the residue (p-dimethylaminobenzoyl chloride) was dissolved in 200 ml anhydrous benzene and the resulting solution with stirring was added drop-wise to a suspension of 20 g lead thiocyanate in 75 ml boiling anhydrous benzene. When the reaction was complete, the precipitate was filtered off and the filtrate was evaporated in vacuum. The residue (11.4 g) was p-dimethylaminobenzoyl isothiocyanate in the form of yellow long needles with m.p. 58-65°, which rapidly reddened in air.

A solution of 7.5 g commercial isothiocyanate in 180 ml anhydrous benzene was added drop-wise with stirring to a boiling solution of 5 g p-phenetidine in 50 ml anhydrous benzene and the reaction mass was then heated for 2 hours more. Upon cooling, the precipitate which separated out was filtered off and washed with benzene.

Yield 8.6 g N-p-dimethylaminobenzoyl-N'-p-ethoxyphenylthiourea with m.p. 178-180.5°. After evaporation, from the mother liquor was isolated an additional 2 g of this substance.

After recrystallization from acetic acid and then from alcohol, we obtained a white crystalline substance with m.p. 181-182°.

Found %: C 62.87; H 6.23; N 12.04. $C_{18}H_{21}O_2N_3S$. Calculated %: C 62.92; H 6.16; N 12.24.

N-p-Acetaminobenzoyl-N'-p-tolylthiourea. a) N-p-Nitrobenzoyl-N'-p-tolylthiourea. To a boiling solution of 9.2 g p-toluidine in 120 ml anhydrous benzene with stirring was added drop-wise in the course of 30 minutes a solution of 17.7 g p-nitrobenzoyl isothiocyanate in 150 ml anhydrous benzene and then the reaction mass was heated for 1 hour more. Upon cooling, the precipitate which separated out was filtered off and washed with benzene. Yield 24.4 g N-p-nitrobenzoyl-N'-p-tolylthiourea in the form of a yellow crystalline substance with m.p. 148-160°. After recrystallization from alcohol, it had m.p. 162-163°.

Found %: C 57.5; H 3.96; N 13.26. $C_{15}H_{13}N_3O_3S$. Calculated %: C 57.2; H 4.15; N 13.33.

b) N-p-Aminobenzoyl-N'-p-tolylthiourea. To a suspension of 19.3 g commercial N-p-nitrobenzoyl-N'-p-tolylthiourea (m.p. 148-160°) in 300 ml ethyl acetate was added 15 g skeletal nickel catalyst (slurry) in alcohol. Hydrogenation was carried out at room temperature and atmospheric pressure for 4 hours. After separation from the catalyst, ethyl acetate was removed in vacuum. The residue (16.9 g) was twice recrystallized from alcohol.

N-p-Aminobenzoyl-N'-p-tolylthiourea was in the form of colorless rectangular flakes with m.p. 191-193°, soluble in dioxane, acetone, ethyl acetate, difficultly soluble in alcohol, insoluble in water.

Found %: C 63.10; H 5.25. N 14.45. $C_{15}H_{15}ON_3S$. Calculated %: C 63.11; H 5.30; N 14.72.

c) N-p-Acetaminobenzoyl-N'-p-tolylthiourea. To a suspension of 3 g N-p-aminobenzoyl-N'-p-tolylthiourea in 40 ml dry chloroform was added, with stirring at room temperature, 2.2 g acetic anhydride.

The reaction mass was boiled on a water bath. Soon all the substance dissolved and then a precipitate again came down. After further heating for 4 hours, the mixture was cooled, the precipitate was filtered off washed with a small quantity of cooled chloroform and dried in a vacuum desiccator. Yield 2.65 g white crystalline substance with m.p. 196-200°.

After two recrystallizations first from glacial and then from 50% acetic acid, it had m.p. 202.5-203.5°.

Found %: C 62.24; H 5.15; N 12.68. $C_{17}H_{17}O_2N_3S$. Calculated %: C 62.35; H 5.23; N 12.84.

Dihydrochloride of N-p-aminobenzoyl-N'-p-aminophenylthiourea. a) N-p-Nitrobenzoyl-N'-p-nitrophenylthiourea. To a boiling suspension of 13.3 g p-nitroaniline in 150 ml anhydrous benzene was added drop-wise in the course of 30 minutes a solution of 20 g p-nitrobenzoyl isothiocyanate in 150 ml anhydrous benzene. After addition of all of the isothiocyanate, the reaction mass was heated for 1 hour more. Upon cooling, the precipitate which separated out was filtered off and washed with benzene.

Yield 30.9 g N-p-nitrobenzoyl-N'-p-nitrophenylthiourea in the form of a yellow crystalline substance with m.p. 181-184°. After subsequent recrystallization from acetic acid and alcohol, it had m.p. 187-189°.

Found %: C 48.55; H 2.88; N 15.70. $C_{14}H_{10}O_5N_4S$. Calculated %: C 48.53; H 2.91; N 16.19.

b) N-p-Aminobenzoyl-N'-p-aminophenylthiourea (dihydrochloride). To a suspension of 28 g commercial N-p-nitrobenzoyl-N'-p-nitrophenylthiourea (m.p. 181-184°) in 400 ml ethyl acetate was added 20 g skeletal nickel catalyst (slurry) in alcohol. Hydrogenation was carried out at room temperature and atmospheric pressure for 8 hours. After filtering off the catalyst, ethyl acetate was evaporated down in vacuum. The remaining crystalline substance — N-p-aminobenzoyl-N'-p-aminophenylthiourea was converted to the dihydrochloride by heating with 10% hydrochloric acid. Upon cooling, colorless crystals in the form of trihedral prisms separated out from the hot solution. After two recrystallizations from dilute hydrochloric acid, the substance had a decomposition temperature above 300°.

Found %: C 47.10; H 4.89; Cl 19.8. $C_{14}H_{14}ON_4S \cdot 2HCl$. Calculated %: C 46.80; H 4.47; Cl 19.73.

Reaction of thiourea with p-phenetidine. a) 4-Ethoxyphenylthiourea. A mixture of 13.7 g p-phenetidine and 7.6 g thiourea was heated for 4 hours at 140°. The mass solidified toward completion of the reaction and was dissolved in 50 ml hot alcohol; the solution was filtered and cooled. The precipitate that separated out (7.5 g) was washed with ether and dried; m.p. 148-157°.

After recrystallization from acetone, we obtained 5.75 g white crystalline substance with m.p. 168-169° (yield 29.3%); after a second recrystallization from alcohol the substance had m.p. 170-171° (literature data give m.p. 172° [12]).

b) 4,4'-Diethoxythiocarbanilide. A mixture of 16 g thiourea and 11.6 g p-phenetidine was heated with stirring for 9 hours at 130-170° and then for 8 hours at 180-210° until evolution of ammonia ceased.

After cooling, the precipitate that separated out was filtered off and washed with cold alcohol; yield 26 g of grey crystalline substance with m.p. 166-169°. Distillation of it in vacuum yielded from the mother liquor 65.5 g unreacted p-phenetidine; thus, the yield of commercial 4,4'-diethoxythiocarbanilide, based on the reacted p-phenetidine, was about 45%.

After two recrystallizations from alcohol, 4,4'-diethoxythiocarbanilide was obtained in the form of colorless lustrous flakes with m.p. 170-171° (the literature data give m.p. 170-171° [3]). A mixed sample with p-ethoxyphenylthiourea was depressed (m.p. 149-154°).

SUMMARY

1. A new series of N'-aryl-N'-aroyl-substituted thioureas is obtained, starting from aromatic acids. The corresponding isothiocyanates are formed intermediately and are condensed with aromatic amines.

2. N-Aryl-N'-aroyl- derivatives of thiourea, containing a nitro group, are reduced to the corresponding amines and their acetyl compounds are prepared.

3. It is established that reaction of equivalent amounts of thiourea and p-phenetidine at 140° gives 4-p-ethoxyphenylthiourea, while with excess of p-phenetidine at 180-210° 4,4'-diethoxythiocarbanilide can be obtained in 45% yield.

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TRIPHENYLPHOSPHAZOSULFONARYLS

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It was recently found that the halogen atoms in trichlorphosphazosulfonaryls are easily replaced by hydroxyls, amino groups [1], alkoxy groups and aryloxy groups [2]. In the present work we show that the halogen atoms of trichlorphosphazosulfonaryls can be readily replaced by aryls with formation of the very little studied and extremely interesting triarylphosphazosulfonaryls according to the scheme:

$$ArSO_2N = PCl_3 + 3Ar'MgBr \rightarrow ArSO_2N = PAr'_3 + 3MgClBr.$$

Elucidation of the structure of the triarylphosphazosulfonaryls obtained by this method was based on the observation that one of them, triphenylphosphazosulfon-p-tolyl, was identical with the triphenylphosphazosulfon-p-tolyl previously [3] prepared from triphenyl phosphite and the sodium salt of the chloramide of p-toluenesulfonic acid according to the scheme:

$$p\text{-}CH_3C_6H_4SO_2NNaCl + P(C_6H_5)_3 \rightarrow NaCl + p\text{-}CH_3C_6H_4SO_2N = P(C_6H_5)_3.$$

This affords adequate proof of its structure as a triarylphosphazosulfonaryl.

EXPERIMENTAL

To 0.15 mole phenylmagnesium bromide, prepared from 0.155 mole bromobenzene and 0.15 mole magnesium in a solution of 100 ml anhydrous ether in an atmosphere of dry hydrogen in the course of 1 hour at room temperature with vigorous mechanical stirring was added a solution of 0.035 mole trichlorphosphazosulfon-p-tolyl in 400 ml absolute ether. The reaction evolved a small amount of heat and the mixture warmed up slightly; the reaction product gradually came down from solution in the form of a viscous mass. After all the trichlorophosphazosulfontolyl solution was added, the reaction mixture was boiled under reflux on a water bath for 2 hours. Then 100 ml saturated aqueous ammonium chloride was added with vigorous stirring. After an hour, the triphenylphosphazosulfon-p-tolyl that came down was suction-filtered off (not separating the layers) and washed with ether (3×15 ml), and water (3×15 ml). Yield 12.6 g. Upon concentration of the ethereal solution, 2.0 g more of less pure product was isolated. Total yield 14.6 g (96.7%). After two recrystallizations from alcohol, triphenylphosphazosulfon-p-tolyl was obtained in the form of colorless fine prisms, m.p. 185-187°.

Found %: N 3.33. $C_{25}H_{22}O_2NSP$. Calculated %: N 3.22.

A mixed sample of the thus-prepared triphenylphosphazosulfon-p-tolyl with the product prepared from triphenylphosphine and sodium p-toluenesulfonchloroamide [3] gave no melting point depression.

The following substances were obtained under these conditions: triphenylphosphazosulfonphenyl, yield 90.0%, crystallized from benzene, fine prisms, m.p. 157-158°.

Found %: N 3.55. $C_{24}H_{20}O_2NSP$. Calculated %: N 3.35.

Triphenylphosphazosulfon-o-tolyl, yield 74.0%, crystallized from a mixture of benzene and carbon tetrachloride (1:1), prisms, m.p. 162-163.5°.

Found %: N 3.25. $C_{28}H_{22}O_2NSP$. Calculated %: N 3.22.

Triphenylphosphazosulfon-α-naphthyl, yield 50.0%, crystallized from alcohol, flat needles, m.p. 200-202°.

Found %: N 3.00. $C_{28}H_{22}O_2NSP$. Calculated %: N 2.99.

Triphenylphosphazosulfon-β-naphthyl, yield 70.0%, crystallized from alcohol, fine prisms, m.p. 162-164°.

Found %: N 2.95. $C_{28}H_{22}O_2NSP$. Calculated %: N 2.99.

The triphenylphosphazosulfonaryls were neutral, colorless, crystalline compounds, odorless, readily soluble at room temperature in chloroform, acetone, dichloroethane, soluble with heating in benzene, methyl and ethyl alcohols, insoluble in carbon tetrachloride and petroleum ether. The triphenylphosphazosulfonaryls were stable to the action of oxidizing agents and hydrolyzed with great difficulty upon boiling with aqueous solutions of acids or alkalis.

SUMMARY

1. Reaction of phenyl magnesium bromide with trichlorphosphazosulfonaryls gives triphenylphosphazosulfonaryls.

2. Some triphenylphosphazosulfonaryls are prepared and their properties are described.

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DI-ACID CHLORIDES OF ACYLAMIDOPHOSPHORIC ACIDS OF THE AROMATIC SERIES

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Under the action of the equivalent amount of water or, better, of anhydrous formic acid, the trichlorophosphazosulfonaryls are easily transformed into the corresponding arylsulfonamidophosphoric acids [1]. The reaction of trichlorophosphazoacyls [2] goes in exactly the same manner with water or with formic acid, with formation of the di-acid chlorides of the acylamidophosphoric acids according to the scheme:

$$ArCON{=}PCl_3 + HCOOH \rightarrow CO + HCl + ArCONHPOCl_2.$$

The reaction is general in character and goes with facility and with very good yields. The di-acid chlorides of acylamidophosphoric acids are crystalline, colorless or light-yellow substances, considerably more resistant to hydrolysis than the corresponding trichlorophosphazoacyls. Thus, for instance, they can be kept for dozens of hours in the air under normal conditions without appreciable decomposition. When heated above the melting point, the di-acid chlorides of acylamidophosphoric acids easily and nearly quantitatively break down to the corresponding nitriles, metaphosphoric acid, phosphorus oxychloride and hydrochloric acid, according to the scheme:

$$2ArCONHPOCl_2 \rightarrow 2ArCN + HPO_3 + POCl_3 + HCl.$$

The di-acid chlorides of acylamidophosphoric acids described in this paper are readily soluble in acetone and rather less soluble in ether and alcohol, with which they slowly react. They crystallize nicely from benzene; they are insoluble in carbon tetrachloride and ligroine. The melting points of the di-acid chlorides of acylamidophosphoric acids are higher than the melting points of the corresponding trichlorophosphazoacyls. Liquid trichlorophosphazoacyls [2] give crystalline dichlorides; the di-acid chlorides of acylamidophosphoric acids can accordingly be successfully used for identification of trichlorophosphazoacyls.

The di-acid chlorides of acylamidophosphoric acids readily enter into reaction with substances containing active hydrogen atoms or metal atoms. The products are the corresponding derivatives of the acylamidophosphoric acids. Thus, for example, with sodium alcoholates and phenolates they give diesters of acylamidophosphoric acids, with amines they give the diamides of acylamidophosphoric acids, etc.

EXPERIMENTAL

The transformation of trichlorophosphazoacyls to acylamidophosphoric acid dichlorides proceeds when finely rubbed trichlorophosphazo compounds are kept for a long period in a thin layer in the air under standard conditions. The transformation goes more rapidly with better yields if the trichlorophosphazoacyls are kept in a desiccator over pulverized caustic potash or caustic soda. In this case the quantity of water is automatically regulated due to the reaction of hydrogen chloride with caustic alkalis. A calculated amount of water may also be added to the benzene solution with vigorous stirring. However, the best results are obtained upon formolysis of trichlorophosphazoacyls in benzene solution.

General method of preparation of aromatic acylamidophosphoric acid dichlorides. To a solution of 0.01 mole trichlorphosphazoacyl in 10-15 ml dry benzene (if necessary, slightly heated) was slowly added drop-wise 0.01 mole anhydrous formic acid. A vigorous reaction immediately started and the mixture warmed up and

carbon monoxide and hydrogen chloride were evolved. Soon, sometimes after cooling, the acid dichloride starts to come down. The product is separated, washed with benzene and, when necessary, recrystallized from benzene. Yields were from 66 to 98% depending on the solubility of the acid dichloride in benzene. When the substance was separated from the mother liquor, the yields in all cases were at least 90-95%.

In this manner the following substances were obtained.

Benzoylamidophosphoric acid dichloride, yield 81.8%; using the mother solution, 92.5%; m.p. 95-96°. This substance was obtained by Titherley and E. Worrel [3] by the action of phosphorus pentachloride and water on benzamide without separation of the intermediate product (trichlorophosphazobenzoyl). Titherley and Worrel report that benzoylamidophosphoric acid dichloride upon "rapid" heating melted with decomposition at 115°. In reality, upon very rapid heating, the melting point of benzoylamidophosphoric acid dichloride depends on the rate of heating and varies in the interval 96-114°, but upon heating at the rate of 1-3° per minute, the substance melts sharply at 95-96°.

Found: equiv.* 4.00, 4.06 (phenolphthalein); 3.01, 2.97 (methyl orange). $C_7H_6O_2NPCl_2$. Calculated: equiv. 4.00 (phenolphthalein); 3.00 (methyl orange).

o-Nitrobenzoylamidophosphoric acid dichloride, light-yellow prisms, yield 92.9%, m.p. 117-118°.

Found %: Cl 25.36, 25.07; equiv. 3.98, 3.96.** $C_7H_5O_4N_2PCl_2$. Calculated %: Cl 25.05; equiv. 4.00.

m-Nitrobenzoylamidophosphoric acid dichloride, light-yellow acicular crystals, yield 98.2%, m.p. 121-122°.

Found %: Cl 24.92; equiv. 4.02, 3.98. $C_7H_5O_4N_2PCl_2$. Calculated %: Cl 25.05; equiv. 4.00.

p-Nitrobenzoylamidophosphoric acid dichloride, light-yellow needles, yield 73.2%, m.p. 130-131°.

Found %: Cl 24.96, 24.99; equiv. 4.04, 4.07. $C_7H_5O_4N_2PCl_2$. Calculated %: Cl 25.05; equiv. 4.00.

2,4-Dinitrobenzoylamidophosphoric acid dichloride, yellow plate-like crystals, yield 94.0%, m.p. 102-104°.

Found %: Cl 21.51, 21.53. $C_7H_4O_6N_3PCl_2$. Calculated %: Cl 21.60.

3,5-Dinitrobenzoylamidophosphoric acid dichloride, light-yellow needles, yield 91.4%, m.p. 167-168°.

Found %: Cl 21.47, 21.65; equiv. 2.96, 3.00 (methyl orange). $C_7H_4O_6N_3PCl_2$. Calculated %: Cl 21.60; equiv. 3.00 (methyl orange).

2-Chloro-4-nitrobenzoylamidophosphoric acid dichloride, light-yellow prisms, yield 66.2%, m.p. 121-122°.

Found %: Cl (hydrolyzed) 22.41, 22.40; equiv. 3.91, 3.97. $C_7H_4O_4N_2PCl_3$. Calculated %: Cl (hydrolyzed) 22.33; equiv. 4.00.

o-Chlorobenzoylamidophosphoric acid dichloride, colorless prisms, yield 85.3%, m.p. 92-93°.

Found %: Cl (hydrolyzed) 25.89, 25.79; equiv. 3.96, 4.03. $C_7H_5O_2NPCl_3$. Calculated %: Cl (hydrolyzed) 26.10; equiv. 4.00.

p-Chlorobenzoylamidophosphoric acid dichloride, colorless needles, yield 81.1% m.p. 106-107°.

Found %: Cl (hydrolyzed) 26.28, 26.10; P 11.10; equiv. 4.03, 4.08. $C_7H_5O_2NPCl_3$. Calculated %: Cl (hydrolyzed) 26.02; P 11.29; equiv. 4.00.

*Equiv. = equivalent after hydrolysis.

**In all cases, except when stated otherwise, the indicator was phenolphthalein.

2,4-Dichlorobenzoylamidophosphoric acid dichloride, colorless fine crystals, yeild 81.4%, m.p. 106-107°.

Found %: Cl (hydrolyzed) 23.11, 23.10; equiv. 4.00, 4.05. $C_7H_4O_2NPCl_4$. Calculated %: Cl (hydrolyzed) 22.96, equiv. 4.00.

Thermal decomposition of benzoylamidophosphoric acid dichloride. 47.6 g (0.2 mole) benzoylamidophosphoric acid dichloride was heated on an oil bath at 150° under reflux for 1 hour. The hydrogen chloride was blown off with dry carbon dioxide and absorbed by alkali solution. The mixture was then fractionated with a Vigreux column (300 mm) at 15 mm. Yield: hydrogen chloride 0.0956 equiv. (95.6%), phosphorus oxychloride 13.3 g (86.9%) and benzonitrile 18.9 g (90.0%).

SUMMARY

Reaction of the equivalent amount of water or, better, of formic acid, with trichlorophosphazoacyls of the aromatic series gives the di-acid chlorides of acylamidophosphoric acids. Their properties are described.

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THE REACTION OF PHOSPHORUS PENTACHLORIDE WITH CARBOXYLIC ACID AMIDES. TRICHLOROPHOSPHAZOACYLS

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The following scheme was proposed by Gerhardt in 1858 [1] for the reaction of phosphorus pentachloride with carboxylic acid amides:

$$RCONH_2 + PCl_5 \rightarrow RCCl_2NH_2 + POCl_3,$$
$$RCCl_2NH_2 \rightarrow HCl + RCCl{=}NH \rightarrow HCl + RCN.$$

This reaction was studied in 1877 by Wallach [2] who unreservedly accepted Gerhardt's scheme although some of his own experimental data could not be satisfactorily explained by Gerhardt's scheme [3]. Subsequently a number of workers occupied themselves with a study of the reaction of phosphorus pentachloride with carboxylic acid amides [4]. None of them, including Wallach, succeeded in isolating a single amide-chloride of the type of $RCCl_2NH_2$ in the pure state. In spite of this, the Wallach-Gerhardt scheme has been generally accepted down to the present day and is cited as fully proven in all handbooks, textbooks and manuals of organic chemistry.

Experimental data conflicting with the Wallach-Gerhardt scheme [5] was recently obtained; a detailed study has therefore been instituted of the reaction of phosphorus pentachloride with carboxylic acid amides.

Amides of some aromatic carboxylic acids were selected as the simplest objects of investigation: amides of benzoic, o-m- and p-nitrobenzoic, 2,4 and 3,5-dinitrobenzoic, 2-chloro-4-nitrobenzoic, o- and p-chlorobenzoic, 2,4-dichlorobenzoic and p-bromobenzoic acids. Under the action of phosphorus pentachloride all these acids give nearly quantitative yields of the corresponding trichlorophosphazoacyls according to the scheme:

$$ArCONH_2 + PCl_5 \rightarrow 2HCl + ArCON{=}PCl_3.$$

An especially close study was made of the reaction with benzoic acid, and it was found that substantially no phosphorus oxychloride is formed; the yields of hydrochloric acid and crude trichlorophosphazobenzoyl are close to the theoretical, and the melting point of the crude trichlorophosphazobenzoyl (58° last crystal) differs from that of the perfectly pure recrystallized product by only 3° (60-61°), which confirms the relatively high purity of the "crude" trichlorophosphazobenzoyl and in turn the nearly quantitative yield of the latter. Amide-chlorides of the type of $ArCCl_2NH_2$ are not formed in the reaction.

The study of the reaction with amides of the other acids (see above) confirmed the results obtained with benzamide.

Consequently it can be considered fully proven that the reaction of phosphorus pentachloride with unsubstituted amides of aromatic carboxylic acids does not go according to the Wallach-Gerhardt scheme but in the same manner as for amides of sulfuric acid, sulfonic acid amides, carbonic acid amides and esters of oxamic acid [5], i.e. with formation of the corresponding trichlorophosphazo compounds.

The trichlorophosphazoacyls of the aromatic series are low-melting crystalline or liquid substances, as a rule readily soluble in benzene, difficultly soluble in ligroine, crystallizing nicely from ligroine or carbon tetrachloride. As far as can be judged from the still small amount of experimental material, ortho-substituted trichlorophosphazoacyls of the aromatic series are liquids. Trichlorophosphazoacyls are remarkably reactive: when

heated to 100-140° they easily split off phosphorus oxychloride and give the corresponding nitriles. This reaction also goes at room temperature under the catalytic action of hydrochloric acid; it is therefore necessary to conduct the synthesis of trichlorophosphazoacyls rapidly under conditions ensuring the quickest and most complete removal of hydrochloric acid. In the absence of hydrochloric acid and of moisture, trichlorophosphazoacyls can be stored unaltered at room temperature for at least several months. They are best stored in a vacuum desiccator over phosphorus pentoxide and pulverized potassium hydroxide. Trichlorophosphazoacyls rapidly hydrolyze when kept over sulfuric acid or potassium hydroxide without phosphorus pentoxide because they "dry" the acid or the alkali.

This behavior is indeed one of the causes of the failure of Wallach's experiments on isolation of the products of interaction of phosphorus oxychloride with carboxylic acid amides. Wallach "dried" and stored all his preparations in desiccators over soda lime, and sometimes he pressed them with filter paper or "dried" them on porous porcelain plate over soda lime [2]. These methods of working and of storing were completely unsuitable for trichlorophosphazo compounds since the latter are easily hydrolyzed by the action of water vapor from the soda lime, so that hydrochloric acid is released, which by reaction with the alkali of the soda lime liberates more water; this results in further hydrolysis of the trichlorophosphazo compound, and the process continues until the product is completely decomposed or until all the alkali has been consumed.

Trichlorophosphazoacyls readily react with water or with formic acid with formation of the di-acid chlorides of acylamidophosphoric acids according to the scheme:

$$ArCON{=}PCl_3 + H_2O \rightarrow HCl + ArCONHPOCl_2,$$

$$ArCON{=}PCl_3 + HCOOH \rightarrow HCl + CO + ArCONHPOCl_2.$$

Further hydrolysis takes place appreciably more slowly.

Trichlorophosphazoacyls react violently with ammonia, amines, alcohols, alcoholates, phenols and other substances containing active hydrogen atoms or metals, with formation of the corresponding compounds; consequently they can serve as starting materials for the preparation of a multitude of diverse derivatives of phosphoric acid of new types.

EXPERIMENTAL

Reaction of phosphorus pentachloride with benzamide. A. Quantitative experiment. 24.2 g dry ground benzamide was mixed with 41.7 g ground phosphorus pentachloride and 40 ml dry carbon tetrachloride in a 0.5 liter two-necked flask. One neck was connected to the source of dry carbon dioxide and the other neck was fitted to the reflux condenser, the upper end of which was connected in sequence to small bubble counter with several drops of sulfuric acid and with a hydrogen chloride absorber containing 0.5 liter water. A weak stream of carbon dioxide (1 bubble per second) was passed and the flask was placed in a water bath, heated to 70°, with constant manual stirring. A vigorous reaction soon began and hydrogen chloride evolved vigorously; evolution was almost at a halt within 7-8 minutes. The reaction was accompanied by considerable absorption of heat. After the vigorous reaction was complete, the rate of carbon dioxide passage was somewhat speeded up and heating to 70° was continued for 15 minutes more until hydrogen chloride had been completely displaced from the flask. The apparatus was then dismantled, the reflux condenser was replaced by a direct condenser and carbon tetrachloride was driven off in vacuum at 30-40°. To remove the last traces of hydrogen chloride and carbon tetrachloride the residue in the flask was heated to 60° under a vacuum of 10 mm for 10-15 minutes. Thus, "crude" trichlorophosphazobenzoyl was obtained which usually, upon cooling, set into a solid crystalline mass with m.p. 58° (the thermometer bulb in the liquid, last crystal). Yield 50.0 g (97.5%).

For purification the substance was dissolved in 50 ml boiling petroleum ether (b.p. 85-95°) and the turbid solution was filtered through a folded filter, which was previously dried in a desiccator over phosphorus pentoxide. Upon cooling (15°), coarse, well-formed, colorless prisms slowly came down which, after several hours, were separated, washed with petroleum ether (three 10-ml portions) and dried in vacuum (2 mm). Yield 34.7 g (67.7%), m.p. 60-61°.

Upon cooling the mother liquor to 0°, 5.4 g more completely pure substance came down. Thus, the total yield of recrystallized trichlorophosphazobenzoyl was 40.1 g (78.1%). Upon concentration, 6-7 g more of less pure product was isolated from the mother liquor. All operations had to be carried out in such a manner that

the substance and its solutions, if possible, were protected from atmospheric moisture.

The yield of hydrogen chloride was determined by titration and was 93-97% of the theoretical.

B. Preparation of trichlorophosphazobenzoyl was most conveniently carried out in a round-bottomed flask, covered by reflux condenser, the upper end of which was connected to a Tishchenko bottle with sulfuric acid. The hydrogen chloride was carried off in a draft. The synthesis and purification of the substance were carried out as in the quantitative experiment.

When the reaction was carried out at lower temperatures and for longer periods of time or when the reaction mixture was left to stand until the solvent was driven off in vacuum, the yields were sharply reduced and even fell to zero, which is due to the action of hydrogen chloride which catalyzes the cleavage of trichlorophosphazoacyls to phosphorus oxychloride and nitriles.

Trichlorophosphazobenzoyl was a colorless crystalline substance, readily soluble in carbon tetrachloride, benzene, dioxane, relatively difficultly soluble in cold petroleum ether.

Found %: Cl 41.30, 41.20; N 5.42, 5.38; P 12.16, 12.21; equiv. acid after hydrolysis (phenolphthalein) 4.97, 4.96. M (in benzene) 265.6, 269.2. $C_7H_5ONPCl_3$. Calculated %: Cl 41.49; N 5.46; P 12.10 equiv. acid after hydrolysis 5.00. M 256.4.

Action of hydrogen chloride and phosphorus pentachloride on trichlorophosphazobenzoyl. In three 50 ml round-bottomed flasks with ground ends was placed 10 ml dry carbon tetrachloride (in each) and 12.8 g trichlorophosphazobenzoyl (in each) with m.p. 60° (last crystal, thermometer bulb in liquid). Then in the course of 15 minutes into the first flask was introduced dry hydrogen chloride with continual manual stirring and then the flask was closed by a ground stopper and set aside at room temperature (20-21°). To the second flask was added 0.6 g carefully ground phosphorus pentachloride and the third flask was used as the control. After 24 hours, carbon tetrachloride and phosphorus oxychloride were driven off from all three flasks in vacuum at 40° and 10 mm (15 minutes) into receivers cooled to -70° (at 10 mm benzonitrile boils at 69.2°, phosphorus oxychloride at 2° and carbon tetrachloride at -19°). After disconnecting the receiver, the second flask was submerged in a bath up to the upper edge of the neck and heated for an additional 20 minutes at 80° and 2 mm in order to sublime the phosphorus pentachloride into the outlet tube. The contents of control flask No. 3 immediately crystallized completely upon cooling and seeding. The weight loss was 0.13 g (1.69%, based on phosphorus oxychloride), m.p. 59° (thermometer bulb in liquid, last crystal). Contents of second flask with phosphorus pentachloride also crystallized immediately and completely. The weight loss was 0.32 g (2.50%, based on phosphorus oxychloride and benzonitrile), m.p. 58°. The contents of the first flask (hydrogen chloride) lost 6.1 g in weight (79.6% based on phosphorus oxychloride) and was a colorless transparent liquid with a strong benzonitrile odor; it did not crystallize upon cooling to -20° even when seeded. After being driven off in vaccum (1 mm, bath 60°) and subsequent distillation, we obtained 2.5 g (48.5%) benzonitrile with b.p. 27-29° (1 mm).

The phosphorus oxychloride found in the distillates was hydrolyzed and the hydrochloric and phosphoric acids which formed were titrated. Thus, in the first distillate we found 6.37 g (83.0%, or 104.2% based on weight loss) phosphorus oxychloride and in the second distillate we found 0.04 g (0.52%, or 20.8% based on the weight loss) and in the third distillate 0.02 g (0.26%, or 15.4% based on weight loss).

The high melting points (58 and 59°) of the products in the second and third flasks and the large divergences between the determinations of the quantity of phosphorus oxychloride by weight loss and by titration (2.50 and 0.52%; 1.69 and 0.26%) shows that the weight loss in the above flasks is caused chiefly by mechanical losses (perhaps by sublimation of the phosphazo compound) and not by cleavage of trichlorophosphazobenzoyl to phosphorus oxychloride and benzonitrile.

The products in the second and third flasks were dissolved in 5 ml carbon tetrachloride and treated with hydrogen chloride as described above. After 24 hours, the carbon tetrachloride and phosphorus oxychloride were driven off. The weight losses corresponded to a cleavage of 86.8 and 92.3%.

Thus, it may be concluded that at room temperature hydrogen chloride greatly accelerates the cleavage of trichlorophosphazobenzoyl to phosphorus oxychloride and benzonitrile.

Thermal cleavage of trichlorophosphazobenzoyl. 25.6 g trichlorophosphazobenzoyl was slowly heated on a bare flame in a round-bottomed flask fitted with a thermometer, the bulb of which is immersed in the fused

substance. Decomposition began at 135-136°. The heat source was immediately removed. The temperature of the liquid rapidly rose to 160° due to the heat of reaction and then began to fall. The reaction mixture was fractionated with a small column. Yield 9.1 g benzonitrile (88.2%) with b.p. 188-192° and 10.9 g phosphorus oxychloride (70.8%).

General method of preparation of aromatic trichlorophosphazoacyls. In a round-bottomed flask fitted with reflux condenser was mixed equimolar quantities of pulverized phosphorus pentachloride and dried ground acid amide and to this was added 5-50 ml dry carbon tetrachloride per each 0.01 mole of reagents. Dry benzene may also be used as a solvent for the reaction with p-nitrobenzamide and 3,5-dinitrobenzamide. After mixing the reagents and the solvent, the flask was immediately placed in a water bath, previously heated to 60-75°. A vigorous reaction immediately began which was complete after 15-20 minutes.

The resulting solution, if necessary, was filtered and the solvent was driven off in vacuum at 60°. The residue consisted of "crude" trichlorophosphazo compounds. The yields approached the theoretical. For purification, the trichlorophosphazoacyls were recrystallized and the liquids were directly analyzed.

When the trichlorophosphazoacyl was rather difficultly soluble in cold carbon tetrachloride (or benzene); after the reaction, the solution was filtered, set aside for crystallization and then the precipitated product was separated off.

In the list of prepared trichlorophosphazoacyls after the name we find the quantities of solvent for the reaction per 0.01 mole, the quantity of solvent for recrystallization per 0.01 mole, yields of recrystallized substances (for crystalline compounds) or the yields of "crude" substances (for liquid compounds), crystalline form and color, melting point and decomposition point. All the prepared trichlorophosphazoacyls were readily soluble in benzene, somewhat more difficultly soluble in carbon tetrachloride, sparingly or insoluble in petroleum ether. In the analytical data equiv. means equivalent of acid after hydrolysis (phenolphthalein). The chlorine content is given in all cases as the hydrolyzed only.

Trichlorophosphazobenzoyl, see above.

Trichlorophosphazo-o-nitrobenzoyl, CCl_4 5 ml; did not crystallize; 100.3%; light-yellow liquid, decomposition temperature 115-120°.

Found %: Cl 34.85, 34.97. Equiv. 5.05, 5.03. $C_7H_4N_2PCl_3$. Calculated %: Cl 35.28. Equiv. 5.00.

Trichlorophosphazo-m-nitrobenzoyl, CCl_4 5 ml; CCl_4 5 ml; 72.0%; light-yellow needles, m.p. 103-105°; decomposition temperature 125-130°.

Found %: Cl 35.45, 35.13; P 9.98, 10.10. Equiv. 4.92, 4.98. $C_7H_4O_3N_2PCl_3$. Calculated %: Cl 35.28; P 10.29. Equiv. 5.00.

Trichlorophosphazo-p-nitrobenzoyl, CCl_4 20 ml; CCl_4 20 ml; 83.0%; light-yellow needles, m.p. 121-123°; decomposition temperature 125-130°.

Found %: Cl 35.14, 35.45; P 10.03, 10.34. Equiv. 5.01, 5.01. $C_7H_4O_3N_2PCl_3$. Calculated %: Cl 35.28; P 10.29. Equiv. 5.00.

Trichlorophosphazo-2,4-dinitrobenzoyl, C_6H_6 7 ml; did not crystallize; 100.2%; light-yellow liquid.

Found %: Cl 30.70, 30.73. $C_7H_3O_5N_3PCl_3$. Calculated %: Cl 30.69.

Trichlorophosphazo-3,5-dinitrobenzoyl, CCl_4 50 ml or C_6H_6 25 ml; CCl_4 50 ml or C_6H_6 25 ml; 89.6 or 88.3%; light-yellow needles, m.p. 125-126°; decomposition temperature 135-140°.

Found %: Cl 30.61, 30.56; P 8.97, 9.00. Equiv. 5.04, 5.03. $C_7H_3O_5N_3PCl_3$. Calculated %: Cl 30.69; P 8.96. Equiv. 5.00.

Trichlorophosphazo-2-chloro-4-nitrobenzoyl, CCl_4 5 ml; did not crystallize; 98.7%; light-yellow liquid, decomposition temperature 100-105°.

Found %: Cl 31.25, 31.52. Equiv. 4.95, 5.01. $C_7H_3O_3N_2PCl_4$. Calculated %: Cl 31.68. Equiv. 5.00.

Trichlorophosphazo-o-chlorobenzoyl, CCl_4 10 ml, did not crystallize; 93.9%; light-yellow liquid.

Found %: Cl 36.39, 36.41. Equiv. 4.96, 5.07. $C_7H_4ONPCl_4$. Calculated %: Cl 36.59. Equiv. 5.00.

Trichlorophosphazo-p-chlorobenzoyl, CCl_4 20 ml; CCl_4 20 ml + 25 ml petroleum ether; 91.9%; colorless needles, m.p. 62-63°; decomposition temperature 105-110°.

Found %: Cl 36.48, 36.56; P 10.60, 10.52. Equiv. 5.02, 5.05. $C_7H_4ONPCl_4$. Calculated %: Cl 36.59; P 10.67. Equiv. 5.00.

Trichlorophosphazo-2,4-dichlorobenzoyl, CCl_4 10 ml; did not crystallize; 98.6%; light-yellow liquid, decomposition temperature 120-125°.

Found %: Cl 32.60, 32.53. Equiv. 4.99, 4.93. $C_7H_3ONPCl_5$. Calculated %: Cl 32.70. Equiv. 5.00.

Trichlorophosphazo-p-bromobenzoyl, CCl_4 10 ml.; petroleumether 5 ml; 47.6%; light-yellow needles, m.p. 64-66°.

Found %: Cl 29.35, 29.62. Equiv. 4.97, 5.04. $C_7H_4ONPCl_3Br$. Calculated %: Cl 29.61. Equiv. 5.00.

Thermal decomposition of trichlorophosphazoacyls. In a test tube was placed about 0.005 mole trichlorophosphazoacyl, the thermometer was lowered so that the mercury reservoir was located in the substance and the reaction mass was slowly heated on a small flame. As soon as the thermal decomposition began, as was indicated by boiling up of the liquid, the external heating was halted. Upon cooling, the reaction mixture was treated with ice water to decompose the phosphorus oxychloride, and the nitrile which came down was separated off, washed with ice water and recrystallized. The known nitriles were identified by melting points and these not described in the literature were analyzed. The decomposition temperatures are given in the list of trichlorophosphazoacyls (see above).

Benzonitrile, see above.

o-Nitrobenzonitrile, 79.5%, m.p. 108-109° [6].

m-Nitrobenzonitrile, 91.0%, m.p. 114-116° [7].

p-Nitrobenzonitrile, 96.0%, m.p. 146-147° [8].

3,5-Dinitrobenzonitrile, 94.6% m.p. 129-130°, light-yellow needles, crystallize from alcohol or from a large quantity of water.

Found %: N 21.70. $C_7H_3O_4N_3$. Calculated %: N 21.76.

2-Chloro-4-nitrobenzonitrile; 94.0%, m.p. 80-81° light-yellow needles, crystallize from alcohol or from a large quantity of water.

Found %: N 15.27. $C_7H_3O_2N_2Cl$. Calculated %: N 15.35.

p-Chlorobenzonitrile, 88.1%, m.p. 91-92° [9].

2,4-Dichlorobenzonitrile, 90.0%, m.p. 60-61° [10].

Preparation of 2,4-dichlorobenzamide. 2,4-dichlorobenzoyl chloride was slowly run with vigorous stirring into a cooled concentrated aqueous solution of ammonia. The amide was separated off, washed with water and dried. Yield 87.4%. After recrystallization from water, 2,4-dichlorobenzamide was in the form of colorless needles with m.p. 181-182°.

Found %: N 7.10. $C_7H_5ONCl_2$. Calculated %: N 7.04.

SUMMARY

1. Amide-chlorides and phosphorus oxychloride are not formed in the reaction of phosphorus pentoxide with unsubstituted amides of aromatic carboxylic acid amides; consequently Wallach's mechanism of this reaction is incorrect.

2. In reality trichlorophosphazoacyls and hydrochloric acid are formed in nearly quantitative yields in the reaction of phosphorus pentachloride with unsubstituted aromatic carboxylic acid amides.

3. Decomposition of trichlorophosphazoacyls by heating gives nitriles and phosphorus oxychloride.

4. The breakdown of trichlorophosphazoacyls into nitriles and phosphorus oxychloride is catalyzed by hydrochloric acid.

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α-NITROACETOPHENONE-o-CARBOXYLIC ACID AND ITS DERIVATIVES

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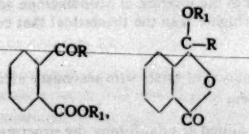
The ability of some aldehydo- and keto- acids to form two series of esters has been repeatedly described in the literature. This relates in particular to aromatic ortho-aldehydo- and ketoacids: phthalic, o-benzoylbenzoic, o-benzylbenzoic, o-aldehydophthalic, opianic and others.

These acids give esters derived from the true open form (I) and from the pseudo form, the lactone (II):



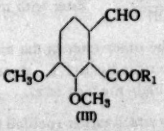
α-form ψ-form

Of the esters of ortho-ketocarboxylic acids, the most thoroughly studied are the derivatives of o-benzoylbenzoic acid. Its methyl and ethyl esters are obtained in the α- and ψ-forms.

The α-methyl ester is obtained by several methods. In particular, from o-benzoylbenzoic acid and diazomethane [1], from its silver salt and methyliodide [2], from the free acid and dimethyl sulfate [1], from its anhydride and sodium methoxide [2], by treatment of the normal acid chloride with methyl alcohol [2]. In all cases one and the same substance with m.p. 52° is formed. Its structure was later verified by various methods, in particular by spectroscopic examination. The ψ-methyl ester is obtained from 2-benzoylbenzoic acid by treatment with thionyl chloride followed by working up with methanol [5]. A similar result is obtained with phosphorus pentachloride. The pseudoester melts at 81°.

Boiling of the ester with m.p. 81° in methanol in presence of a little sulfuric acid or thionyl chloride converts it into the open α-form with m.p. 52° [3].

Of the ortho-aldehyuocarboxylic acids, the most studied have been the esters of opianic acid (III),

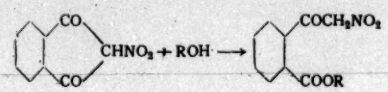


(III)

which likewise exist in two isomeric forms. The α-methyl ester is obtained from the silver salt and methyl iodide [6], by the action of diazomethane on the acid [7], by the action of methanol on the product of reaction of the acid with phosphorus pentachloride [8]. In all cases a substance with m.p. 82-84° is formed to which the α-structure is assigned. The ψ-methyl ester is obtained by boiling the acid with methanol [9]. M.p. 103-104°. The reciprocal transition of the two forms of the ester has been studied by Rodionov and Fedorov [10].

We have published a paper [11] giving preliminary data for the products of reaction of 2-nitroindandione-

1,3 with methanol and ethanol. The reaction went smoothly according to the scheme



and led respectively to the methyl ester of α-nitroacetophenone-o-carboxylic acid with m.p. 108-109° and to the ethyl ester with m.p. 82-83°; on saponification with caustic alkalies these in turn gave good yields of the acid itself.

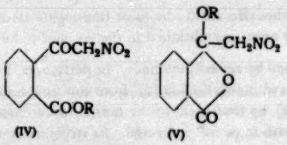
Vanag and Gudrinietse [12] later studied the reaction of 2-nitroindandione-1,3 with secondary alcohols but obtained less satisfactory results.

When heated in an alcoholic medium, 2-nitroindandione-1,3 probably hydrolyzes to α-nitroacetophenone-o-carboxylic acid under the catalytic action of its hydrogen ions •, and the resultant carboxylic acid is esterified also under the catalytic action of the hydrogen ions.

This interpretation of the mechanism of the reaction is supported, firstly, by the fact that addition of α-nitroacetophenone-o-carboxylic acid to the mixture of nitrodiketone and alcohol considerably increases the yield of ester, the total amount of which is higher than the theoretical that could have been formed from 2-nitroindandione-1,3 alone.

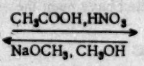
Secondly, the difficulty of formation of esters with secondary alcohols is consistent with the ideas about the occurrence of an esterification reaction.

In the present investigation we aimed at establishing the structure of these esters since two formulas (IV, V) can be proposed for them:



(IV) (V)

In a study of the properties of the methyl ester with m.p. 108-109°, it was converted into the other isomeric ester by the action of a mixture of glacial acetic acid and concentrated nitric acid. The isomeric ester melted at 115-116°, gave on saponification the same α-nitroacetophenone-o-carboxylic acid, and by the action of sodium methoxide was quantitatively converted into the original ester with m.p. 108-109°.



Ester with m.p. 108-109° Ester with m.p. 115-116°.

This observation prompted a search for the other ester in the mother liquors from recrystallization of the ester with m.p. 108-109° obtained from 2-nitroindandione-1,3, since the acid, which is a nitrodiketone, could have partly isomerized the low-melting ester to the high-melting form.

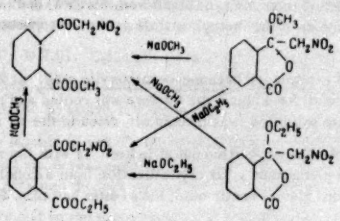
This theory was confirmed. Fractional crystallization enabled isolation of a considerable quantity of the isomers of the previously described methyl and ethyl esters. The isomer of the methyl ester with m.p. 108-109° melted as before at 115-116°; the ethyl ester with m.p. 82-83° had m.p. 96°.

We studied the behavior of these two pairs of esters towards cold 5% sodium bicarbonate solution. It was

• G. Vanag showed that 2-nitroindandione-1,3 behaves in aqueous solution like a strong acid equal in strength and properties to hydrochloric acid [13].

found that both of the low-melting forms slowly dissolved with liberation of carbon dioxide, but the high-melting forms were completely insoluble under these conditions. The two first substances were recovered unchanged after acidification of sodium bicarbonate solutions with mineral acids. This quite decisively solves the problem of their structure, the low-melting esters having the open structure (IV) and the high-melting esters the cyclic structure (V).

A study was also made of the action of alcoholates on both forms. The following scheme illustrates the mutual transitions which proceed with quantitative yields.



Consequently the alcoholates act by cleaving the lactone ring of the pseudo form.

As already mentioned, α-nitroacetophenone-o-carboxylic acid is easily obtained in good yield from the esters. Boiling with acetic anhydride leads to formation, also in good yield, of the previously difficultly accessible nitromethylene phthalide, the starting substance for the synthesis of isocoumarin [14].

EXPERIMENTAL

1. Isomeric methyl esters of α-nitroacetophenone-o-carboxylic acid. a) Separation of esters by means of an aqueous solution of sodium bicarbonate. 22.3 g 2-nitroindandiondione-1,3 was covered with 100 ml methanol and boiled on a water bath for 4 hours. After cooling, the yellow transparent solution was poured into 1 liter of cold water and set aside overnight. When dry, the crystalline powder weighed 15.5 g. For separation of the isomeric esters the powder was vigorously shaken for 15 minutes at room temperature with 200 ml 5% solution of sodium bicarbonate; evolution of carbon dioxide gas was noted and a portion of the substance slowly passed into solution giving it a weak yellow-greenish color. The precipitate was then filtered off, again treated in the same way with bicarbonate solution and again filtered off. The residue on the filter was dried and recrystallized from alcohol. Yield 5.7 g of substance or 26%, based on the initial nitrodiketone*. M.p. 115-116°. Recrystallization from water did not change the melting point.

Found %: C 53.75; H 4.16; N 6.42. $C_{10}H_9O_5N$. Calculated %: C 53.81; H 4.03; N 6.28.

The soda extract was acidified with dilute sulfuric acid, the precipitate of β-ester which came down was filtered off and dried. The weight of dry substance was 7 g. M.p. 107-108°. After recrystallization from alcohol, it had m.p. 108-109°. Recrystallization from water did not change the melting point. Yield of β-ester was 32%.

Found %: C 53.89; H 3.99; N 6.21. $C_{10}H_9O_5N$. Calculated %: C 53.81; H 4.03; N 6.28.

b) Separation of esters by fractional crystallization from ethyl alcohol. 20 g 2-nitroindandione-1,3 was boiled with 100 ml methyl alcohol for 1.5 hours. Upon cooling the reaction solution and rubbing with a glass rod, the first crystal fraction came down and was separated and dried. Weight 7 g. After two recrystallizations from alcohol, the α-ester was obtained with m.p. 107-108°.

The methanolic mother liquor from the first fraction was diluted with water until slight turbidity and then set aside to crystallize. After three recrystallizations from ethyl alcohol, we obtained 1.5 g substance with m.p. 100-110°. Upon recrystallization from acetic acid in which the α-form was more soluble, we obtained the pure

* 2-Nitroindandione-1,3 contains 2 molecules of water.

ψ-ester with m.p. 115-116°. The α- and ψ-methyl esters crystallized very well from alcohol, quite readily from water and acetic acid; withstood boiling in methanol and ethanol for a very long period without showing signs of reciprocal transformation.

The pure α-form is readily soluble in bicarbonate from which is separates out quantitatively. The ψ-form is absolutely insoluble in bicarbonate.

2. Preparation of methyl esters in presence of α-nitroacetophenone-o-carboxylic acid. 7 g 2-nitroindandione-1,3 and 7 g α-nitroacetophenone-o-carboxylic acid were boiled with 100 g methanol on a water bath for 3 hours. Upon cooling, we obtained 10.3 g crystalline product with m.p. 80-90°. After treatment with soda, the insoluble precipitate of pseudomethyl ester, recrystallized from alcohol, had m.p. 115-116°. Upon acidification, the soda solution gave a white powder of the methyl ester of α-nitroacetophonone-o-carboxylic acid with m.p. 107-108°.

3. Isomeric ethyl esters of α-nitroacetophenone-o-carboxylic acid. a) 20.5 g 2-nitroindandione-1,3 was boiled with 100 ml anhydrous alcohol for 4 hours; the mixture was cooled and poured into 1 liter of cold water. After 12 hours, the oily precipitate solidified, was filtered off, dried in the air and pulverized.

The treatment with soda solution was carried out as in Item 1a with the sole difference that it was repeated not 2 but 4 times. The insoluble precipitate, after crystallization from alcohol, had m.p. 94-95°. Weight 2.6 g (12%). After recrystallization from glacial acetic acid, the ψ-ester had m.p. 95-96°.

Found %: 55.68; H 4.41; N 6.26. $C_{11}H_{11}O_5N$. Calculated %: 55.71; H 4.62; N 5.91.

Upon acidification of the soda solution, a white precipitate of the α-ester came down. After recrystallization from alcohol, the substance weighed 7.6 g (36%). M.p. 82-83°.

Found %: C 55.80; H 4.44; N 5.92. $C_{11}H_{11}O_5N$. Calculated %: C 55.71; H 4.62; N 5.91.

4. Reaction of ester with sodium alcoholates. a) Transesterification of esters. 5 g α-ethyl ester with m.p. 82-83° was dissolved in 50 ml 3% sodium methylate solution in methanol. After 1-2 minutes, a crystalline precipitate of salt came down. After acidification, the mixture gave a white crystalline powder of α-methyl ester. The yield was quantitative. M.p. 107-108° (from alcohol). When sodium methylate was replaced by the ethylate the α-ethyl ester remained unchanged.

b) Action of sodium methylate on ψ-methyl ester. 2 g ester with m.p. 115-116° was dissolved in 10 ml 3% sodium methylate inmethanol. The substance rapidly dissolved, giving the solution a yellow color. Upon acidification of the reaction mixture, we obtained a white powder. Recrystallization from alcohol yielded only a product with m.p. 107-108°. The yield was 1.6 g. The obtained substance mixed with the known ester (m.p. 108-109°) melted without depression; with the product of isomerization (m.p. 115-116°) it gave a depression and melted at 89-100°.

c) Action of sodium ethylate on ψ-methyl ester. 0.6 g ψ-methyl ester was covered with 3% sodium ethylate in ethanol. After acidification with dilute sulfuric acid, white powder of the ester was recrystallized from alcohol. M.p. 82-83°. The substance melted without depression with the previously prepared α-ethyl ester.

d) Action of sodium methylate on ψ-ethyl ester. 1.5 g ψ-ethyl ester with m.p. 95-96° was treated as in Item b. After recrystallization from alcohol, we obtained the α-methyl ester with m.p. 108-109° which melted without depression with the previously prepared α-methyl ester.

e) Action of sodium ethylate on ψ-ethyl ester. After solution of the ψ-ethyl ester in 3% sodium ethylate, we obtained a quantitative yield of α-ethyl ester with m.p. 82-83° (from alcohol). A mixture with the initial product melted without depression (at 65-75°).

5. Isomerization of α-esters to ψ-esters in a mixture of acetic and nitric acids. a) 6 g methyl ester of α-nitroacetophenone-o-carboxylic acid with m.p. 107-108° was dissolved in 50 ml glacial acetic acid. To the solution was added a mixture of 10 ml glacial acetic acid and 8 ml nitric acid, spec. grav. 1.52. After standing for 12 hours, the mixture was diluted with water, and the white powder, after drying, was recrystallized from alcohol from which it crystallized very well. Yield 3 g, m.p. 115-116°. The second recrystallization did not change the melting point. The mixture with the initial substance had m.p. 88-94°. The substance remained unchanged upon being boiled for 6 hours in methanol.

b) 2 g α-ethyl ester with m.p. 82-83° was dissolved in a mixture of 20 ml glacial acetic acid and 4 ml nitric acid, spec. grav. 1.40. The mixture stood for 24 hours. After dilution, fractional crystallization yielded a very small quantity of ester with m.p. 95-96°.

6. α-Nitroacetophenone-o-carboxylic acid. 50 g α-methyl ester was suspended in 50 ml 5% caustic soda solution. Upon vigorous shaking, the substance gradually dissolved at room temperature with a slight yellow coloration until it completely dissolved. After filtration, the solution was acidified with concentrated hydrochloric acid. After 10 minutes, the milk-white liquid gave a white well-formed crystalline precipitate. It was separated off and dried in the air. Weight 44 g (94%). M.p. 121-122°. After recrystallization from water, it had m.p. 133-134°. Recrystallization from benzene and xylene did not change the melting point.

Found %: C 51.65; H 3.20; N 7.01. $C_9H_7O_5N$. Calculated %: C 51.68; H 3.35; N 6.70.

Determination of active hydrogen (Chugaev-Tserevitinov). Found %: active H 0.98, 0.92; number of active H 2.03, 1.87. $C_9H_7O_5N$. Calculated %: active H 0.95; number of active H 2.00.

The substance was readily soluble in water with an acid reaction. Upon boiling with hydrochloric acid, it gave phthalonic acid, identified via 3-phenylphthalazone-4-(1)-carboxylic acid with m.p. 216°. In mixture with the known preparation, the obtained product melted without depression.

The α-ethyl ester similarly, and in the same yield, gave the same product. The mixture of both samples melted without depression. Saponification of the pseudo forms yields the same acid with m.p. 133-134°.

The acid is quite resistant to alkali. For example, upon brief boiling in 2% caustic soda solution, it remained unchanged and only more prolonged boiling destroyed it. Phthalic acid was one of the decomposition products.

7. Esterification of α-nitroacetophenone-o-carboxylic acid. 5 g acid was boiled in methyl alcohol which contained several drops of concentrated sulfuric acid on a water bath, in a flask fitted with reflux condenser. After being boiled for 2 hours, the reaction mixture was diluted with water. The coarse crystalline white powder was separated off and dried in air. Weight 5 g. After recrystallization from alcohol, the white needles melted at 107-108° and were the α-methyl ester of α-nitroacetophenone-o-carboxylic acid. The mixture with the known substance melted without depression.

8. Preparation of nitromethylenephthalide from α-nitroacetophenone-o-carboxylic acid. 11 g α-nitroacetophenone-o-carboxylic acid was boiled with 50 ml acetic anhydride for one and one half hours. Cooling yielded a large amount of dark-yellow crystals. After separation and drying, we obtained 6 g (60%) of substance with m.p. 205-206°. With known nitromethylene phthalide it gave no melting point depression.

The filtrate was diluted with water and after hydrolysis of acetic anhydride, a yellow powder came down with m.p. 150-153°. After two recrystallizations from alcohol, we obtained beautiful yellow crystals with m.p. 153°.

Found %: N 7.59. $C_9H_5O_4N$. Calculated %: N 7.33.

When the substance with m.p. 153° was again boiled for 2 hours in acetic anhydride, it converted to nitromethylene phthalide with m.p. 206-207°.

SUMMARY

A method is developed for the preparation of α-nitroacetophenone-o-carboxylic acid and its esters, and of nitromethylene phthalide. The structure of the prepared compounds is established.

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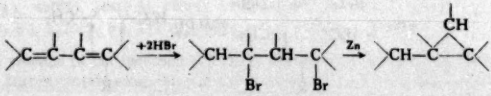
SYNTHESIS OF HYDROCARBONS

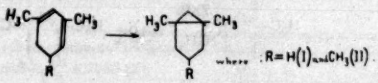
LIV. TRANSFORMATION OF HYDROCARBONS OF THE CYCLOHEXADIENE SERIES INTO BICYCLIC HYDROCARBONS CONTAINING A THREE MEMBERED RING – (0,1,3)-BICYCLOHEXANES

R. Ya. Levina, Kim Dyai Gir and E. G. Treshchova

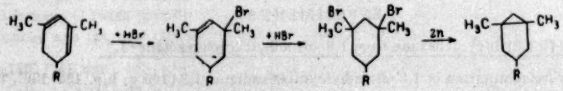
In the years 1949 to 1952 one of us [1] developed a new reaction which was associated with the simple transition of dienic hydrocarbons to cyclopropanes. The reaction consists in the exhaustive hydrobromination of dienic hydrocarbons and cyclization of the 1,3-dibromides with zinc dust:



In the present work this reaction is applied for the first time to cyclic dienic hydrocarbons – homologs of cyclohexadiene:



The starting substances were 1,3-dimethylcyclohexadiene-1,3 and 1,3,5-trimethylcyclohexadiene-1,3; addition of one molecule of hydrobromic acid to these hydrocarbons leads to formation of only one hydrobromide of the allylic type, regardless of whether hydrobromination occurs in the 1,2-or the 1,4-position [2]; addition of a second molecule of hydrobromic acid gives the ditertiary 1,3-dibromide which under the action of zinc is transformed into a bicyclic hydrocarbon of the (0,1,3)-bicyclohexane series:

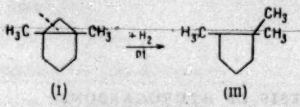


By this route we prepared 1,3-dimethyl-(0,1,3)-bicyclohexane (R = H) and 1,3,5-trimethyl-(0,1,3)-bicyclohexane (R = CH_3) in yields (after distillation of the reaction products in a column) of 25.5% and approx. 10% respectively, calculated on the starting cyclohexadienic hydrocarbon.

The presence of a three-membered ring in the prepared bicyclic hydrocarbons was confirmed by exami-

nation of their Raman spectra and also by their behavior when catalytically hydrogenated.

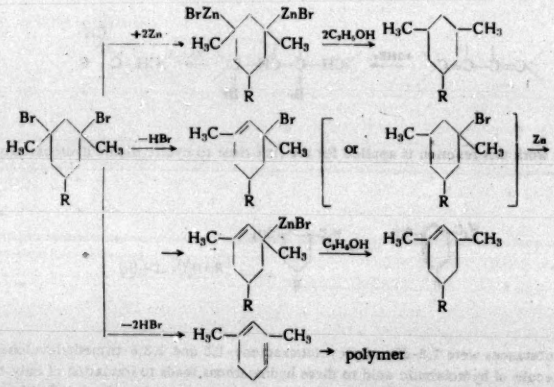
Hydrogenation of 1,3-dimethyl-(0,1,3)-bicyclohexane (I) over platinized carbon at 120° led to formation of 1,1,2-trimethylcyclopentane(III), constants and Raman spectra of which agreed completely with the literature data:



(I) (III)

Consequently the opening of the three-membered ring in dimethylcyclohexane by its catalytic hydrogenation is accompanied by formation of a cyclopentanic and not of a cyclohexanic hydrocarbon, similarly to what was observed by N. D. Zelinsky and B. A. Kazansky [3] in the hydrogenation of thujane.

The action of zinc on the dihydrodibromides of cyclohexadienes (1,3-dibromocyclohexanes) leads, apart from the normally proceeding Gustavson reaction, to secondary processes [4] of reduction and dehydrobromination – reduction of the 1,3-dibromide (with zinc dust and alcohol) to a cyclohexanic hydrocarbon, cleavage of one molecule of hydrobromic acid from the 1,3-dibromide and subsequent reduction of the resultant unsaturated monobromide to a cyclohexenic hydrocarbon, and also the cleavage of two molecules of hydrobromic acid from the 1,3-dibromide with formation of the original cyclohexadienic hydrocarbon which later partially polymerizes:



Formation of these secondary products was also responsible for the low yield (25.5% and approx. 10%) of our newly synthesized bicyclic hydrocarbons with a three-membered ring – 1,3-dimethyl- and 1,3,5-trimethyl-(0,1,3)-bicyclohexane.

EXPERIMENTAL

1,3-Dimethyl-(0,1,3)-bicyclohexane from 1,3-dimethylcyclohexadiene-1,3

Exhaustive hydrobromination of 1,3-dimethylcyclohexadiene-1,3 (105 g; b.p. 135-136°, 755 mm, n_D^{20} 1.4872 [2]) was carried out with ice-salt cooling. The obtained dihydrodibromide (1,3-dibromo-1,3-dimethylcyclohexane) was dissolved in alcohol and reacted with zinc dust. The reaction was carried out in a 3-necked flask fitted with mercury-sealed stirrer, dropping funnel (with jacket for ice cooling) and condenser. To 375 g zinc dust in 560 ml alcohol (95%) with vigorous stirring and ice-salt cooling was slowly added an alcoholic solution of dibromodimethylcyclohexane, cooled with ice in a dropping funnel. After addition of the dibromide was complete, the reaction mixture was stirred for 2 hours more with cooling, 5-6 hours at room temperature and 2 hours with heat-

ing on a water bath. The hydrocarbons which formed were driven off together with alcohol from the reaction flask, were then separated out from alcoholic solution by addition of water, were washed with water, dried with calcium chloride and distilled over sodium (total yield 81 g, 76.4%).

After the first distillation over sodium of the obtained hydrocarbon mixture on a column of 35 theoretical plates, we isolated three fractions, 109-110° (23 g), 110-126° (27 g) and 126-140° (25 g). A resinous residue remained in the distilling flask. After a subsequent fractional distillation on the same column, we obtained the following fractions: 1st 27 g, 109-110° (748 mm), n_D^{20} 1.4358; 2nd 3.5 g, 110-120° (758 mm), n_D^{20} 1.4340; 3rd 4.2 g, 120-120.5° (758 mm), n_D^{20} 1.4318; 4th 3.2 g, 120.5-124.8° (758 mm), n_D^{20} 1.4400; 5th 3.3 g, 124.8-125° (758 mm), n_D^{20} 1.4447; 6th 30 g, 125-140°, n_D^{20} 1.4630.

The 1st fraction, judging by its physical and chemical properties (see below) was 1,3-dimethyl-(0,1,3)-bicyclohexane (yield 27 g, 25.5%, based on the initial dimethylcyclohexadiene) and after a repeated distillation, had the following constants:

B.p. 110° (768.5 mm), n_D^{20} 1.4360, d_4^{20} 0.8056, MR_D 35.76. C_8H_{14}. Calc. 35.44. Found %: C 87.12, 87.27; H 12.74, 12.83. C_8H_{14}. Calculated %: C 87.19; H 12.81.

1,3-Dimethyl-(0,1,3)-bicyclohexane is not described in the literature.

The Raman spectrum of the obtained hydrocarbon was recorded on a "Shteinkhel" spectrograph with a slit width of 6 cm^{-1}; the intensity of the lines was measured visually in a conditional scale in which the intensity of the frequency 1450 cm^{-1} was taken as 10 units:

307(0), 340(3.5; g), 455(1), 516(0.5), 602(2), 621(0.5), 677(15), 793(1.5), 824(0.5), 884(4), 928(2), 978(0.5), 1015(2.5; b), 1102(2.5; b), 1170(2; b), 1192(1), 1227(2; b), 1290(2), 1364(0.5), 1389(1.5), 1450-1463(10; b).

Judging from the absence in the spectrum of lines in the region 1600 cm^{-1}, the isolated 1,3-dimethyl-(0,1,3)-bicyclohexane did not contain admixtures of 1,3-dimethylcyclohexene; the spectrum also lacked lines characteristic for the cis-and trans-forms of 1,3-dimethylcyclohexane [5]: 752(123), 1056(26), 1262(28) for one form and 419(38), 546(47), 771(58), 1059(36) for the other.

The 3rd fraction (4.2 g; about 4%, based on initial diene) had a low refractive index in comparison to the lower- and higher-boiling fraction, which indicated that it contained cyclohexane hydrocarbon; it had a boiling point near that of the boiling point of the trans-form* of 1,3-dimethylcyclohexane: b.p. 120-120.5° (758 mm), n_D^{20} 1.4318, d_4^{20} 0.7783.

Literature data for trans-1,3-dimethylcyclohexane*: b.p. 121° (760 mm), n_D^{20} 1.4269, d_4^{20} 0.774 [6], b.p. 120.4-120.6° (760 mm), n_D^{20} 1.4230, d_4^{20} 0.7666 [5].

Table 1 gives the Raman spectra of the fraction with b.p. 120-120.5° and for comparison gives the literature data for the cis- and trans-forms of 1,3-dimethylcyclohexane.

The presence in the spectrum of the most intense lines of the trans*-form of 1,3-dimethylcyclohexane (bold face in table) indicates that fraction 120-120.5° was mainly trans-1,3-dimethylcyclohexane which formed due to the side process of reduction with an admixture of up to 10% 1,3-dimethylcyclohexene or 1-methyl-3-methylenecyclohexane (line 1647 cm^{-1} in spectrum) and possibly of cis*-1,3-dimethylcyclohexane (to 5%; line 746 cm^{-1} in spectrum).

5th fraction (3.3 g; about 3%, based on initial diene), judging from its constants and Raman spectrum, was 1,3-dimethylcyclohexene-1 (with possible admixture of 1,3-dimethylcyclohexenes with the double bond in another position) which formed as a result of side processes of dehydrobromination and reduction:

B.p. 124.8-125° (758 mm), n_D^{20} 1.4447, d_4^{20} 0.8006, MR_D 36.61; Calc. 36.47. Found %: C 87.08, 87.04; H 13.03, 13.25. C_8H_{14}. Calculated %: C 87.19; H 12.81.

* The works of Rossini and Pitzer [7] note that the trans-form of 1,3-dimethylcyclohexane described in the literature is really the cis-form and vice-versa.

TABLE 1

Combined Dispersion Spectra

Fraction with b.p. 120-120.5°	1,3-Dimethylcyclohexane [5]	
	trans-forms *	cis-forms *
170(0.8), 254(1), 340(0.5)	254(6)	314(0), 355(4)
377(0.8), **413-420**(5; b)	**409**(13), **419**(38)	375(4), 438(0)
452(1.8), 494(0.8), **547**(5.5)	450(13), **546**(47)	455(19), 488(8.9)
565(0), 586(0), 609(2.5)		626(13)
674(1), 709(0.5), 746(1.5)	748(0)	**752**(123)
769(15), 822(0.5), 850(2)	**771**(58), 829(1), 849(1)	802(3), 841(0)
889(1; b), 929(0.5; b), 956(0.1)	880(0), 934(3), 955(3)	862(10.3), 935(13)
970(0.5), 983(1), 1014(0)	983(13), 1000(5)	981(8), 1007(13)
1056(3), 1080(1), 1107(3; b)	**1059**(36), 1079(2), 1112(5)	1020(0), 1056(26), 1075(8)
1165(7), **1183**(2), 1219(2.5)	**1166**(22), **1179**(22), 1219(12)	1101(11), 1164(17)
1267(2.5)	1268(11)	1212(2.5), 1262(28)
1304(1), **1342**(4; b), 1460(10;b)	1303(7.7), 1340(22), 1460(50)	1308(4), 1330(4)
1647(3)		1364(3), 1460(42)

Literature data [8]: b.p. 124-126° (760 mm), n_D^{20} 1.4487, d_4^{20} 0.8006.

The Raman spectrum of the isolated 1,3-dimethylcyclohexene is given below:

170(0.5), 276(1), 224(0),333(0.5),380(0.5;V), 434(1), 457(1.5), 485(1), 545(1.5), 594(2), 623(2), 663(0.8), 695(0.8), 718(0.5), 746(3), 773(3.5; b), 808(2.5), 845(0.6), 889(0), 978(0), 1073(1.5; g), 1104(2.5), 1136(0.1), 1165(3.5), 1183(0.5), 1267(0.8), 1296(2), 1326(2), 1347(1.5), 1382(0.5), 1427(8), 1460(10; g), 1640(0.3), 1672(10).

The 6th fraction (30 g; 30% of initial diene), as its constants show, contained the product of the complete dehydrobromination of the dibromide—1,3-dimethylcyclohexadiene.

The hydrogenation of 1,3-dimethyl-(0,1,3-)-bicyclohexane (8.1 g) was carried out over platinized carbon (15% Pt) in a stream of hydrogen (the rate of passage of the hydrocarbon was 0.1 ml per minute) at 120°. After distillation on a column, the resulting catalyzate had constants corresponding to the constants of 1,1,2-trimethylcyclopentane:

B.p. 111.5-111.8° (730 mm), n_D^{20} 1.4238, d_4^{20} 0.7751, MR_D 36.93; calc. 36.94. Found %: C 85.99, 85.79; H 14.27, 14.13. C_8H_{16}. Calculated %: 85.62; H 14.37.

Literature date for 1,1,2-trimethylcyclopentane: b.p. 114° (755 mm), n_D^{19} 1.4234, d_4^{19} 0.7719 [9], b. p. 113.7° (750 mm), n_D^{20} 1.4228, d_D^{20} 0.7728 [10].

The second possible product of hydrogenolysis of the three-membered ring is 1,3-dimethylcyclohexane which has a boiling point that is considerably higher (from 120 to 125° [11] for the cis- and trans-forms).

Table 2 gives the Raman spectra that we obtained for 1,1,2-trimethylcyclopentane (the spectrum was recorded under the above-described conditions) and of the Fenske preparation [10].

It is apparent from the data of Table 2 that all the lines of highest and mean intensities in the given spectra of 1,1,2-trimethylcyclopentane are in agreement. The spectral investigation of the obtained hydrocarbon confirmed the absence in it of admixed 1,3-dimethylcyclohexane.

1,3,5-Trimethyl-(0,1,3)-bicyclohexane.

The ditertiary dibromide prepared from 1,3,5-trimethylcyclohexadiene-1,3 (225 g; b.p. 146-147°, n_D^{20} 1.4770 [12]) was reacted with zinc dust in alcoholic solution under the conditions cited above. The hydrocarbon mixture obtained from six experiments (each time 30-40 g trimethylcyclohexadiene was taken for the hydrobromination reaction), after the usual treatment and distillation over sodium (total yield 120 g) was fractionally distilled on a column; 1,3,5-trimethyl-(0,1,3)-bicyclohexane (20 g; about 10%) was isolated and had the following constants:

*See footnote p. 1047.

B.p. 125-125.5° (735 mm) n_D^{20} 1.4335, d_4^{20} 0.7994, MR_D 40.42. $C_9H_{16}\Delta$. Calc. 40.06. Found %: C 86.91, 86.88; H 12.97, 13.08. C_9H_{16}. Calculated %: C 87.01; H 12.99.

1,3,5-Trimethyl-(0,1,3)-bicyclohexane is not described in the literature.

Raman spectrum: 242(1; b), 307(0), 373(1.2), 417(1.5), 451(0.3), 529(0.5), 547(3), 586(0), 635(2; b), 693(12; b), 808(2), 843(1), 860(5), 912(1), 970(1), 1022(1.5), 1037(1), 1056(0), 1085(1.8), 1102(1.2), 1144(4), 1164(2.5), 1183-1193(2; b), 1227(6), 1277(7; b), 1342(7), 1384(4), 1440-1460(10; b).

It is evident from the given spectrum that the isolated 1,3,5-trimethyl-(0,1,3)-bicyclohexane did not contain admixed 1,3,5-trimethylcyclohexene (lines were absent in the region 1600 cm^{-1}).

TABLE 2

Raman Spectrum of 1,1,2-Trimethylcyclopentane

Obtained in the present work	Literature date [10]
257—276(0.5; b), 357(1), 373(0.5)	273(23), 358(42)
504(2.5), 547(0.5), 621(0.8), 671(1)	507(43), 548(15), 616(30)
695(5; b), 714(1), 795(0.5)	692(112)
833(1.8; b), 889(8), 930(2), 957(1)	832(45), 890(136), 935(74)
970(0), 1014(1.5), 1056(1), 1093(7; db)	1010(38), 1060(46), 1097(42)
1183(2; b; g), 1196(2; b; g), 1230(0.8)	1182(21), 1230(60)
1270—1296(1; g), 1322(0.7)	1286(29), 1348(25)
1382(1; b; g), 1440—1460(10; b)	1397(15), 1458(168)

Distillation of the obtained hydrocarbon mixture on a column did not effect a separation of the side reaction products of dehydrobromination and reduction—1,3,5-trimethylcyclohexane and 1,3,5-trimethylcyclohexene, since the first of them could exist in two stereoisomeric forms (cis- and trans-) and the second could exist in several isomeric forms, differing in position of the double bond in the ring and in spatial arrangement of the methyl groups.

After two fractional distillations, beside trimethylbicyclohexane (1st fraction, b.p. 125-125.5°), the following close-boiling fractions were collected (a non-distilling resinous residue remained in the distilling flask): 2nd 7.5 g, 125.5-130° (735 mm), n_D^{20} 1.4355; 3rd 6.2 g, 130-138° (735 mm), n_D^{20} 1.4373; 4th 10 g, 138-139° (735 mm), n_D^{20} 1.4408; 5th 7.6 g, 139-140° (735 mm), n_D^{20} 1.4420; 6th 13.8 g, 140-141° (734 mm), n_D^{20} 1.4445; 7th 17.6 g, 141-141.3° (734 mm), n_D^{20} 1.4470; 8th 15 g, 141.3-150° (734 mm), n_D^{20} 1.4680. Fractions 4-7 contained, apparently, mainly isomeric and stereoisomeric 1,3,5-trimethylcyclohexenes (in each of the Raman spectra of the 4th and 7th fractions the frequencies 1644 and 1668 cm^{-1} appeared) with possible admixture of 1,3,5-trimethylcyclohexanes. According to literature data, 1,3,5-trimethylcyclohexene-1 has b.p. 139-141° (760 mm) and $n_D^{24.7}$ 1.44378 [13], b.p. 142.5-143.5° (760 mm) and n_D^{21} 1.447 [14]; 1,3,5-trimethylcyclohexane (a mixture of cis- and trans-forms) has b.p. 137-138° (752 mm) and n_D^{20} 1.4268 [15], b.p. 137.8-139° (747 mm) and n_D^{20} 1.4280 [5].

Judging from its constants, the 8th fraction contained initial 1,3,5-trimethylcyclohexadiene-1,3 (about 7% of that taken for reaction).

SUMMARY

1. In a continuation of previous studies on the transformation of dienic hydrocarbons into cyclopropanic hydrocarbons, a new method of synthesis of bicyclic hydrocarbons containing a three-membered ring — (0,1,3)-bicyclohexanes — was developed. This consists in exhaustive hydrobromination of cyclohexadienes-1,3 and cleavage of two bromine atoms with zinc dust (Gustavson reaction) from resultant ditertiary 1,3-dibromocyclohexanes.

2. The new method was applied to the synthesis of the previously undescribed 1,3-dimethyl-(0,1,3)-bicyclohexane (yield 25.5%) from 1,3-dimethylcyclohexadiene-1,3 and of 1,3,5-trimethyl-(0,1,3)-bicyclohexane (yield about 10%) from 1,3,5-trimethylcyclohexadiene-1,3.

3. The low yield of (0,1,3)-bicyclohexanes is due to the fact that the action of zinc on the ditertiary 1,3-dibromide of the cyclohexane series results, apart from the Gustavson reaction, in secondary processes of reduction and dehydrobromination on a considerable scale, which lead to formation of the original cyclohexadienes as well as of cyclohexenic and cyclohexanic hydrocarbons.

4. The presence of a three-membered ring in the synthesized (0,1,3)-bicyclohexanes was confirmed by their physical properties (constants and Raman spectra) and chemical properties (catalytic hydrogenation).

5. Catalytic hydrogenation of 1,3-dimethyl-(0,1,3)-bicyclohexane at 120° over platinized carbon causes rupture of the three-membered ring and leads to formation of a cyclopentanic hydrocarbon (1,1,2-trimethylcyclopentane), which was confirmed by the Raman spectrum of the catalyzate.

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TETRAACYLOXYSILANES IN THE SYNTHESIS OF α, β-UNSATURATED ACIDS

I. SYNTHESIS OF CINNAMIC ACID

Yu. K. Yuryev, G. B. Elyakov and A. N. Vysokosov

In 1868 W. Perkin established that coumarin was formed when the sodium derivative of salicylaldehyde was heated with acetic anhydride [1]. Later study of this reaction led to the discovery of a new method of preparation of cinnamic acid by reaction of benzaldehyde (1 mole) with acetic anhydride (1.5 moles) in presence of anhydrous sodium acetate (0.65 mole) with heating for 7-8 hours at 175-180°; the yield of acid was 48-52%. Homologs and derivatives of cinnamic acid are obtained by this method by heating a mixture of aromatic aldehyde, aliphatic acid anhydride and sodium salt of the same acid.

$$C_6H_5CHO + (RCH_2CO)_2O \xrightarrow{RCH_2COONa} C_6H_5CH{=}\underset{R}{C}{-}COOH + RCH_2COOH.$$

Many publications have been devoted to the study of the mechanism of this reaction [2-6].

There are indications [7] of the possibility of slightly raising the yield of cinnamic acid if the amount of sodium acetate is increased to 1 mole, but further increase (to 2 moles) no longer appreciably influences the yield of acid. Introduction of more than 1.5 moles acetic anhydride likewise does not usually give an appreciable increase in the yield of acid [7]. Performance of the reaction in indifferent solvents (toluene, nitrobenzene) lowers the yield of cinnamic acid and may even stop the reaction entirely. It was also established [7] that the yield of cinnamic acid rises with increasing duration of heating at 180°.

According to the data of Meyer and Beer [8] a higher yield of cinnamic acid (72%) can be obtained if potassium acetate is used in place of sodium acetate.

Kalinin [6] showed that salts of other acids can be used successfully in Perkin's reaction; an example is potassium carbonate (yield of cinnamic acid 59%); tertiary amines are also condensing agents in Perkin's reaction, and their activity rises with increasing basicity of the amine; nevertheless the best results are obtained with potassium acetate.

Recently mixed anhydrides of orthosilicic acid and monobasic organic acids (tetraacyloxysilanes) have been used successfully in place of acid chlorides or of anhydrides for acylation of phenols [10] and in the Gustavson-Friedel-Crafts reaction for acylation of benzene and toluene [10], and also (as shown by us) for the acylation of thiophene [11] and selenophene [12].

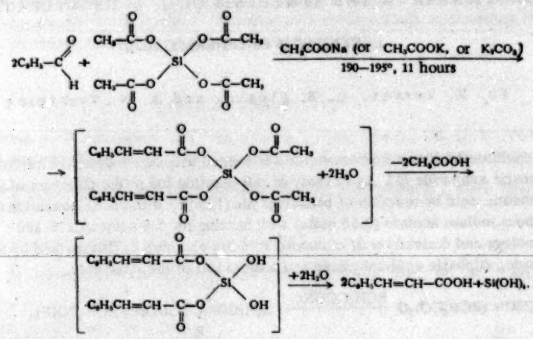
We also showed that mixed anhydrides of silicic and dibasic organic acids are more convenient acylating agents for the preparation of ketonic acids of the benzene series [13] and of thiophene [14] than the usually employed anhydrides of dibasic acids or their acid chlorides, or the acid chlorides of their acid ethyl esters.

Since the silicoanhydrides of organic acids behave in the above acylation reactions exactly like anhydrides of organic acids, it was of the utmost interest to study the possibility of employing silicoanhydrides of monobasis acids for the preparation of aromatic α,β-unsaturated acids. A successful outcome in this case would permit the introduction of tetraacyloxysilanes into condensations of this type, i.e. the utilization of the labile hydrogen atoms of their α-methylene group.

In the present work we established that in the synthesis of cinnamic acid silicoacetic anhydride is completely equivalent to acetic anhydride and that the condensation of benzaldehyde with silicoacetic anhydride is realized in the presence of the same condensation agents (sodium acetate, potassium acetate, potassium

carbonate). In this reaction it was shown that in silicoacetic anhydride and in other silicoanhydrides of aliphatic acids, the lability of the hydrogen atoms of the α-methylene group is not inferior to the lability of the hydrogen atoms in the α-methylene group of the anhydride of the corresponding acid, and that in condensations with participation of such an α-methylene group it is possible to replace the anhydrides of the acids by the more accessible and more easily prepared silicoanhydrides of organic acids.

Our described condensation of benzaldehyde with tetraacetoxysilane (silicoacetic anhydride), leading to cinnamic acid, may be represented by the following extremely probable scheme:



According to our proposed reaction scheme, the water released in the condensation partially hydrolyzes the mixed silicoanhydride of acetic and cinnamic acids with formation of acetic acid and the partial mixed anhydride of orthosilicic and cinnamic acids (or, what is also possible , with formation of cinnamic acid and the partial mixed anhydride of orthosilicic and acetic acids).

After investigating in detail the reaction with respect to amounts of components, nature of the condensing agents, temperatures and durations of heating, we found that the maximum yield of cinnamic acid (74.5 %) is attained after 11-hour heating at 190-195° of 1 mole benzaldehyde with 1.2 moles silicoacetic anhydride in presence of 1 mole anhydrous potassium acetate (table, Experiment 9). Results obtained in experiments with other ratios of reactants, other condensing agents and with a different duration of heating are set forth in the table.

Since we know from the literature data that silicoacetic anhydride breaks down on heating to 179-180° with formation of acetic anhydride and silica [9], we checked the correctness of our proposed reaction mechanism by carrying out the condensation at a lower temperature which ruled out the possibility of appreciable decomposition of the silicoacetic anhydride. It was found that heating of the mixture of benzaldehyde, silicoacetic anhydride and anhydrous potassium acetate at 135° for 25 hours (table, Experiment 5) likewise leads to formation of cinnamic acid (yield 52%).

In the reaction described, therefore, benzaldehyde condenses with silicoacetic anhydride itself, although this by no means excludes the possibility of its partial decomposition at a temperature of the order of 180° and of the partial participation of the resultant acetic anhydride in the reaction.

In the experimental part we present procedures permitting the attainment of maximum yields of cinnamic acid on condensation of benzaldehyde with tetraacetoxysilane in presence of potassium acetate, sodium acetate and potassium carbonate as condensing agents.

Tetraacetoxysilane in the Synthesis of Cinnamic Acid

Reactants and experimental conditions	Number of experiment and amounts of reactants																							
	1		2		3		4		5		6		7		8		9		10		11		12	
	g	mole	g	mole	g	mole	g	mole	g	mole	g	mole	g	mole	g	mole	g	mole	g	mole	g	mole	g	mole
Benzaldehyde	21.2	0.2	16.0	0.15	10.6	0.1	19.2	0.18	10.6	0.1	21.2	0.2	10.6	0.1	10.6	0.1	21.2	0.2	10.6	0.1	10.6	0.1	10.6	0.1
Silicoacetic anhydride	40.0	0.15	31.0	0.11	26.4	0.1	70.0	0.26	26.4	0.1	40.0	0.15	19.8	0.076	26.4	0.1	65.0	0.24	25.4	0.1	33.	0.12	39.6	0.15
Excess of silica (in %)	–	50	–	50	–	100	–	170	–	100	–	50	–	50	–	100	–	140	–	100	–	150	–	200
Sodium acetate	10.0	0.13	12.3	0.15	8.2	0.1	16.5	0.2	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Potassium acetate	–	–	–	–	–	–	–	–	9.8	0.1	19.6	0.2	9.8	0.1	9.8	0.1	19.6	0.2	–	–	–	–	–	–
Potassium carbonate	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	13.8	0.1	13.8	0.1	13.8	0.1
Temperature (in bath)	190-195°		190-195°		190-195°		190-195°		130-135°		190-195°		190-195°		190-195°		190-195°		190-195°		190-195°		190-195°	
Duration of heating (in hours)	7.5		12		12		12		25		8		11		11		11		11		11		11	
Yield of cinnamic acid	8 g (27%)		10.7 g (48%)		7.4 g (50%)		17 g (64%)		7.8 g (52%)		15 g (50.5%)		9 g (60%)		10.4 g (70%)		22.1 g (74.5%)		7.4 g (50%)		9.1 g (61.5%)		9.6 g (63%)	

Note. Experiment 1 was performed without stirring of the reaction mixture.

EXPERIMENTAL

Tetraacetoxysilane was obtained in the form of a white crystalline mass as described by Friedel and Ladenburg [9]. It must be noted, howevever, that occasionally tetraacetoxysilane did not crystallize and remained in the form of a very viscous syrup, but in the synthesis of cinnamic acid it gives the same results as the crystalline compound.

Procedure. In a 100ml round-bottomed flask, fitted with reflux condenser with mechanical stirrer passing through it, was placed 0.1-0.2 mole benzaldehyde and respectively 0.1-0.24 mole tetraacetoxysilane and 0.1-0.2 mole potassium acetate, sodium acetate or potash. The reaction mixture was heated on an oil bath to 190-195° and in the initial period of the reaction the reaction mass usually solidified but softened again after 10-15 minutes of heating at 200°. In certain cases when the hardening at 200° could not be counteracted, the temperature of the oil bath was raised to 220-230°. Heating at 190-195° with stirring was continued for 11-12 hours and then the reaction mass was cooled and decomposed with hot water. The reaction mass was then alkalized and the unreacted benzaldehyde was driven off with steam. Activated carbon was then added to the residue in the flask and it was filtered while hot. The precipitate of silicic acid on the filter was then washed twice with a 2 N solution of caustic soda and cinnamic acid was separated out from the filtrate by careful acidification with concentrated hydrochloric acid. Cinnamic acid was usually obtained completely pure and had a sharp melting point.

1. From 21.2 g benzaldehyde and 65 g tetraacetoxysilane in presence of 19.6 g freshly-melted and rubbed (to a powder) potassium acetate was obtained 22.1 g (74.5%) cinnamic acid: m.p. 133° (table, Experiment 9).

2. From 19.2 g benzaldehyde and 70 g tetraacetoxysilane in presence of 16.5 g freshly-melted and rubbed (to a powder) sodium acetate was obtained 17 g (64%) cinnamic acid: m.p. 133° (table, Experiment 4).

3. From 10.6 g benzaldehyde and 39.6 g tetraacetoxysilane in presence of 13.8 g calcined and rubbed (to a powder) potash we obtained 9.6 g (63%) cinnamic acid: m.p. 133° (table, Experiment 12).

A mixing test of the obtained acid from each experiment with known cinnamic acid gave no melting point depression.

SUMMARY

It was established that the silicoanhydrides of monobasic aliphatic acids, which are true mixed anhydrides, can enter into condensation with aldehydes and yield α,β-unsaturated acids.

Taking tetraacetoxysilane (silicoacetic anhydride) as a model substance, it is shown that it can successfully replace acetic anhydride in the synthesis of cinnamic acid; the resultant yields of acid (when using potassium acetate, sodium acetate or potassium carbonate as condensing agents) are not lower than those reported in the literature for synthesis of cinnamic acid with the help of acetic anhydride.

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* T.p. = C. B. Translation pagination.

THE CHEMISTRY OF SELENOPHENE

II*. ACYLATION OF 3,4-DIMETHYLSELENOPHENE WITH TETRAACYLOXYXILANES

Yu. K. Yuryev and N. K. Sadovaya

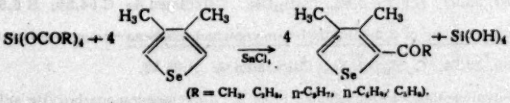
Acylation of homologs of selenophene with the help of anhydrides of chlorides of monobasic organic acids has been described by E. G. Kataev and M. V. Palkina [1] who acylated 2-methyl- and 2,5-dimethylselenophene with acetic anhydride in presence of phosphoric acid and obtained 2-methyl-5-acetylselenophene and 2,5-dimethyl-3-acetylselenophene, respectively, in yields of 50 and 44.4 %.

A paper by Buu-Hoi et al.[2] described the acylation of 2,4-diphenylselenophene with acetyl chloride and propionyl chloride. Due to the presence of phenyl radicals in the 2,4-positions of the selenophene ring, its acylation was possible not only in presence of anhydrous tin chloride but also of anhydrous aluminum chloride which usually causes considerable destruction of selenophene itself and complete destruction of its homologs. The yields of ketones obtained in the different cases are very similar and amount to 75% on the average.

In the preceding paper [3] one of us established that the acetylation of selenophene itself can be easily and conveniently performed with the help of silicoanhydrides of monobasic organic acids (tetraacyloxysilanes) in presence of anhydrous tin chloride. The corresponding alkyl- and arylselenienyl ketones were obtained in higher yields (70-80%) than in the case of acylation with acid chlorides (yield 42%) [4] or with anhydrides (yield 32-50%) [1], as described in the literature[1].

In the present work it is shown that silicoanhydrides of monobasic organic acids can be successfully employed also for the acylation of homologs of selenophene, for example, 3,4-dimethylselenophene.

Acylation of 3,4-dimethylselenophene with tetraacyloxysilanes in presence of anhydrous tin chloride under conditions in which selenophene itself underwent acylation proceeded with lower yields but nevertheless reached 50%. By acylation of 3,4-dimethylselenophene in this manner, we obtained the previously undescribed 3,4-dimethyl-2-acetoselenophene, 3,4-dimethyl-2-propioselenophene, 3,4-dimethyl-2-n-butyroselenophene, 3,4-dimethyl-2-n-valeroselenophene and 3,4-dimethyl-2-cyclopentanoylselenophene.



(R = CH_3, C_2H_5, n-C_3H_7, n-C_4H_9, C_5H_9).

* Communication I see Proc. Acad. Sci. USSR, 102, 763 (1955).

EXPERIMENTAL

Procedure. To a 3-necked flask (50 ml), fitted with stirrer, dropping funnel and reflux condenser with calcium chloride tube, was added 30 ml absolute benzene, 0.05 mole acid, 0.025 mole silicon tetrachloride and the reaction mixture was heated on a water bath first at 60-70° and then on a boiling water bath until complete cessation of hydrogen chloride evolution. The reaction mass was then cooled with ice and 0.013 mole anhydrous stannic chloride was immediately added, upon which the reaction mixture usually darkened somewhat. Upon stirring and cooling with ice water, a solution of 0.025 mole 3,4-dimethylselenophene in 10 ml absolute benzene was added drop-wise in the course of 15 minutes. Toward completion of addition of 3,4-dimethylselenophene a complex formed which was dark-brown, almost black, in color. Refrigeration was then stopped and the mixture was stirred for 15 minutes at room temperature and then heated for 15 minutes on a water bath at 60-70°. The reaction mass was cooled, poured in ice water and set aside overnight for complete decomposition of the complex. Upon distillation with superheated (300°) steam, the ketone came over in negligible quantity with the benzene that first came over and most of it separated out in the aqueous distillate as a heavy light-yellow oil. The benzene layer was separated off, the aqueous layer was saturated with table salt and extracted 3 times with ether. The ether-benzene extracts were dried with calcium chloride, the solvents were driven off and the ketone was vacuum-distilled in a stream of nitrogen or recrystallized from 45% alcohol.

3,4-Dimethyl-2-acetoselenophene. From 3 g acetic acid, 4.3 g silicon tetrachloride and 3.9 g 3,4-dimethylselenophene in presence of 3.1 g stannic chloride was obtained 2.6 g (50%) ketone with m.p. 52-53°.

Found %: C 47.94, 47.73; H 5.10, 5.09. $C_8H_{10}OSe$. Calculated %: C 47.78; H 5.01.

2,4-Dinitrophenylhydrazone of 3,4-dimethyl-2-acetoselenophene – red crystals with m.p. 223°.

Found %: N 14.48, 14.44. $C_{14}H_{14}O_4N_4Se$. Calculated %: N 14.70.

3,4-Dimethyl-2-propioselenophene. From 3.7 g propionic acid, 4.3 g silicon tetrachloride and 3.9 g 3,4-dimethylselenophene in presence of 3.1 g stannic chloride was obtained 2.4 g (49%) ketone with m. p. 53-54°.

Found %: C 50.25, 50.27; H 5.77, 5.83. $C_9H_{12}OSe$. Calculated %: C 50.24; H 5.63.

2,4-Dinitrophenylhydrazone of 3,4-dimethyl-2-propioselenophene – red-violet crystals with m. p. 214°.

Found %: N 14.61, 14.44. $C_{15}H_{16}O_4N_4Se$. Calculated %: N 14.18.

3,4-Dimethyl-2-n-butyroselenophene. From 4.4 g n-butyric acid, 4.3 g silicon tetrachloride and 3.9 g 3,4-dimethylselenophene in presence of 3.1 g stannic chloride was obtained 3 g (53%) ketone:

B.p. 134.5-135.5° (10 mm), n_D^{20} 1.5568, d_4^{20} 1.2952, MR_D 56.94. $C_{10}H_{14}OSe$. Calc. 55.86.
Found %: C 52.27, 52.29; H 6.20, 6.27. $C_{10}H_{14}OSe$. Calculated %: C 52.47; H 6.16.

2,4-Dinitrophenylhydrazone of 3,4-dimethyl-2-n-butyroselenophene – red crystals with m. p. 146°.

Found %: N 13.71, 13.74. $C_{16}H_{18}O_4N_4Se$. Calculated %: N 13.69.

3,4-Dimethyl-2-n-valeroselenophene. From 5.1 g n-valeric acid, 4.3 g silicon tetrachloride and 3.9 g 3,4-dimethylselenophene in presence of 3.1 g stannic chloride was obtained 2.9 g (48%) ketone:

B. p. 151.5-152.5° (14 mm); n_D^{20} 1.5548, d_4^{20} 1.2660, MR_D 61.15. $C_{11}H_{16}OSe$. Calc. 60.59.
Found %: C 53.87, 53.89; H 6.74, 6.82. $C_{11}H_{16}OSe$. Calculated %: C 54.30; H 6.63.

2,4-Dinitrophenylhydrazone of 3,4-dimethyl-2-n-valeroselenophene – orange-red crystals; m. p. 125°.

Found %: N 13.39, 13.24. $C_{17}H_{20}O_4N_4Se$. Calculated %: N 33.23.

3,4-Dimethyl-2-cyclopentanoylselenophene. From 5.7 g cyclopentanecarboxylic acid, 4.3 g silicon tetrachloride and 3.9 g 3,4-dimethylselenophene in presence of 3.1 g stannic chloride was obtained 3 g (48%) ketone:

B. p. 172.5-173° (11 mm), n_D^{20} 1.5792, d_4^{20} 1.3170, MR_D 64.45. $C_{12}H_{16}OSe$. Calc. 62.90.
Found %: C 56.61, 56.87; H 6.50, 6.50. $C_{12}H_{16}OSe$. Calculated %: C 56.48; H 6.32.

2,4-Dinitrophenylhydrazone of 3,4-dimethyl-2-cyclopentanoylselenophene – yellow crystals with m. p. 103°.

Found %: N 12.46, 12.67. $C_{18}H_{20}O_4N_4Se$. Calculated %: N 12.90.

SUMMARY

Silicoanhydrides of organic acids (tetraacyloxysilanes) are convenient agents for the acylation of selenophene and its homologs.

Acylation of 3,4-dimethylselenophene with the silicoanhydrides of acetic, propionic, n-butyric, n-valeric and cyclopentanecarboxylic acids gave, for the first time, 3,4-dimethyl-2-acetoselenophene; 3,4-dimethyl-2-propioselenophene; 3,4-dimethyl-2-n-butyroselenophene; 3,4-dimethyl-2-n-valeroselenophene; and 3,4-dimethyl-2-cyclopentancylselenophene.

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ORGANOCYCLOSILOXANES

I. METHYLCHLOROCYCLOSILOXANES

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Organosilicon alkyl(aryl)halosilanes hydrolyze fairly easily to form cyclic polymers. Thus, the hydrolysis of dimethyldichlorosilane gave [1,2] methylcyclosiloxanes of the $[(CH_3)_2SiO]_n$ series, where n = 3-8. The preparation was likewise carried out of hexaethylcyclotrisiloxane, octaethylcyclotetrasiloxane, decaethylcyclopentasiloxane [3], tri(methylphenyl)cyclosiloxane and tetra(methylphenyl)cyclotetrasiloxane [4], hexaphenylcyclosiloxane and octaphenylcyclotetrasiloxane [5], butoxycyclosiloxanes of the $[(C_4H_9O)_2SiO]_{3-8}$ series [6], etc.

Hydrogen-containing cyclic organopolysiloxanes of the $[CH_3SiO]_{4-6}$ (H) series were obtained by hydrolysis of methyldichlorosilane [7]. In this case the cyclic trimer was isolated in extremely small yield; it could only be obtained [8] from the products of breakdown of the cyclic polymers. Hydrolysis of ethyldichlorosilane gave [9] cyclic compounds of the $[C_2H_5SiO]_{3-6}$ (H) series.

Each of these compounds has two organic radicals at the silicon atom, or an organic radical and a hydrogen. We investigated the chlorination of methylcyclosiloxanes with the objective of obtaining methylchlorocyclosiloxanes and of studying their properties. Apart from that, we attempted to isolate higher methylcyclosiloxanes of the $[CH_3SiO]_n$ (H) series.

The experiments showed that hydrolysis of methyldichlorosilane gives, apart from the cyclic compounds described in the literature: 1) heptamethylcycloheptasiloxane $[CH_3SiO]_7$ (H) with b. p. 114° (21 mm), m. p. −82°, n_D^{20} 1.3982 and d_{20}^{20} 1.0142, and 2) octamethylcyclooctacyclohexane $[CH_3SiO]_8$ (H) with b. p. 105° (2 mm), m. p. −64°, n_D^{20} 1.4010, d_{20}^{20} 1.0218.

In the chlorination of hydrogen-containing methylcyclosiloxanes the hydrogen in the Si-H bond is quantitatively replaced by chlorine according to the equation:

$$[CH_3SiO]_n (H) + nCl_2 \rightarrow [CH_3SiO]_n (Cl) + nHCl$$

With the help of this reaction we obtained the products of successive chlorination and of complete chlorination of methylcyclosiloxanes of the $[CH_3SiO]_{4-7}$ (H) series (Table 1). They are, with the exception of tetra(methylchloro)tetracyclosiloxane, colorless liquids. All the prepared methylchlorocyclosiloxanes, like the organochlorosilanes, are easily hydrolyzed even by moisture from the air.

In the diagram the change of melting points of methylchlorocyclosiloxanes is compared with that of dimethylcyclosiloxanes [2] and with that of methylcyclosiloxanes [7] ([7] and our data).

The diagram shows that replacement of a methyl radical or a hydrogen atom in the Si-H linkage by chlorine does not alter the regularity of fall of melting points of cyclic compounds containing an odd number of silicon atoms.

EXPERIMENTAL

Preparation of methylcyclosiloxanes. The starting product was methyldichlorosilane CH_3SiHCl_2 with b. p. 41° (found%: Cl 62.26; H 0.92; calculated %: Cl 61.74; H 0.86). Hydrolysis of methyldichlorosilane was carried out in a glass hydrolyzer fitted with stirrer and a jacket for water-cooling. Upon vigorous stirring,

TABLE 1

Methylchlorocyclosiloxanes

Methylchlorocyclosiloxanes	Formula	Boiling point (pressure in mm in parentheses)	Melting point	d_{20}^{20}	Yield (%)
1,3,5,7-Tetramethyl-1-chloro-cyclotetrasiloxane	$[CH_3SiO]_4H_3Cl$	150-152°	−55°	1.0977	–
1,3,5,7-Tetramethyl-1,5-chloro-cyclotetrasiloxane	$[CH_3SiO]_4H_2Cl_2$	88(30)	−7.5	1.1786	–
1,3,5,7-Tetramethyl-1,3,5-chloro-cyclotetrasiloxane	$[CH_3SiO]_4HCl_3$	101(30)	2	1.2562	–
Tetra(methylchloro)cyclotetra siloxane	$[CH_3SiOCl]_4$	220(745)	76	–	97
Penta(methylchloro)cyclopenta-siloxane	$[CH_3SiOCl]_5$	~250	−55	1.3372	99
Hexa(methylchloro)cyclohexa-siloxane	$[CH_3SiOCl]_6$	~276	−10	1.3391	98
Hepta(methylchloro)cycloheptа-siloxane	$[CH_3SiOCl]_7$	~308	−25	1.3434	92

100 g of CH_3SiHCl_2 was run in the course of 30 minutes from a dropping funnel into the mixture of 200 g ethyl alcohol and 200 ml water in the hydrolyzer. The temperature during hydrolysis was held at 15-18°. When hydrolysis was complete, the alcohol-aqueous layer was separated off, the hydrolysis products were washed several times with water until the reaction for HCl was neutral and they were filtered several times for drying. Yield of polymethylsiloxanes 50 g (96%).

850 g polymethylsiloxanes were obtained in all of which 300 g volatile (cyclic) compounds was obtained by vacuum distillation. Fractionation on a vacuum column of 10 theoretical plates yielded methylcyclosiloxanes. Octamethylcyclooctasiloxane was isolated by distillation of the still residue from a Wurtz flask.

Tetramethylcyclotetrasiloxane: b. p. 134° (746 mm), n_D^{20} 1.3890. Found %: H (−Si) 1.61. M 242. Calculated %: H (−Si) 1.68. M 240.4. Pentamethylcyclopentasiloxane: b. p. 85° (43 mm), n_D^{20} 1.3930. Found %: H (−Si) 1.65. M 307. Calculated %: H (−Si) 1.68. M 300.5. Hexamethylcyclohexasiloxane: b. p. 105° (32mm), n_D^{20} 1.3960. Found %: H (−Si) 1.60. M 357. Calculated %: H (−Si) 1.68. M 360.6.

Heptamethylcycloheptasiloxane. Found %: H (−Si) 1.62; C 21.22; H 6.97; Si 46.64. M 422, MR 99.74. Calculated %: H (−Si) 1.68; C 20.00; H 6.66, Si 46.66. M 420, MR 99.89.

Octamethylcyclooctasiloxane. Found %: H (−Si) 1.62; C 19.91; H 6.59; Si 46.33. M 481, MR 114.20. Calculated %: H (−Si) 1.68; C 20.00; Si 46.66. M 480, MR 114.16.

Preparation of methylchlorocyclosiloxanes. Gaseous dry chlorine was passed through the solution of the corresponding methylcyclosiloxane in CCl_4 located in the reaction vessel with the jacket for water-cooling *. The tube along which the chlorine passed was lowered to the bottom of the vessel. The temperature was regulated by a thermometer immersed in the chlorinated product and was held at 20 to 30°. The chlorine was passed at a rate of about 0.01 liter per minute. The end of the reaction was indicated by the drop in temperature despite an increase in the rate of chlorine delivery and by yellowing of the product due to its saturation with an excess of gaseous chlorine. After the reaction was complete, the carbon tetrachloride, excess of chlorine and HCl were driven off in vacuum up to 100°. The products of complete and partial chlorination of tetramethyl-cyclotetrasiloxane were again subjucted to rectification in vacuum on a column (of 10 theoretical plates).

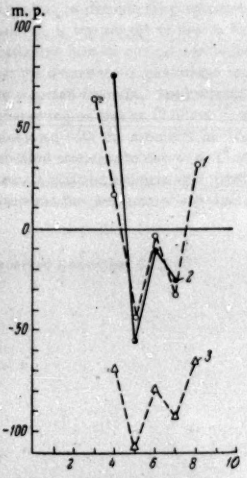
* The chlorination reaction proceded exothermally. The preliminary experiments showed that chlorination of pure methylcyclosiloxanes goes so vigorously that the temperature and course of the reaction cannot be regulated.

The analytical data are given in Table 2.

TABLE 2

Analysis of Methylchlorocyclosiloxanes

Methylchlorocyclosiloxanes	Content in %											
	C		H		C		H		C		H	
	calc.	found	calc.	found	calc.	found	calc.	found	calc.	found	calc.	found
$[CH_3SiO]_3H_2Cl$	17.85	17.71	5.46	5.30	12.93	12.81	40.80	40.62	1.09	0.99	274.5	272
$[CH_3SiO]_3H_1Cl_2$	15.53	15.48	4.53	4.56	22.97	22.98	36.24	36.10	0.50	0.70	309.0	305
$[CH_3SiO]_3HCl_3$	13.97	13.88	3.78	3.66	31.00	30.94	32.71	32.71	0.29	0.32	343.5	345
$[CH_3SiO]_4$ Cl	12.69	12.45	3.17	3.19	37.56	36.32	29.62	29.90	0	0	378.0	380
$[CH_3SiO]_5$ Cl	12 69	12.18	3.17	2.94	37.56	36.00	29.62	28.52	0	0	472.0	472
$[CH_3SiO]_6$ Cl	12.69	12.70	3.17	3.20	37.56	36.50	29.62	29.27	0	0	567.0	550
$[CH_3SiO]_7$ Cl	12.69	12.60	3.17	3.22	37.56	38.41	29.62	29.65	0	0	661.0	669



Number of Si-O linkages

Melting points: 1) of dimethylcyclosiloxanes, 2) of methylchlorocyclosiloxanes, 3) of methylcyclosiloxanes.

SUMMARY

1. The following new cyclic compounds were synthesized and characterized – methylchlorocyclosiloxanes: 1,3,5,7-tetramethyl-1-chlorocyclotetrasiloxane, 1,3,5,7-tetramethyl-1,5-chlorocyclotetrasiloxane, 1,3,5,7-tetramethyl-1,3,5-chlorocyclotetrasiloxane, tetra-(methylchloro)cyclotetrasiloxane, penta(methylchloro) cyclopentasiloxane, hexa(methylchloro)cyclohexasiloxane, hepta(methylchloro)-cycloheptasiloxane.

2. New compounds were isolated: heptamethylcycloheptasiloxane and octamethylcyclooctasiloxane.

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All-Union Electrotechnical Institute

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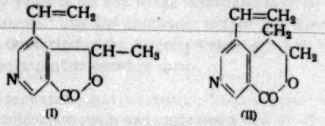
THE PROBLEM OF THE STRUCTURE OF GENTIANINE

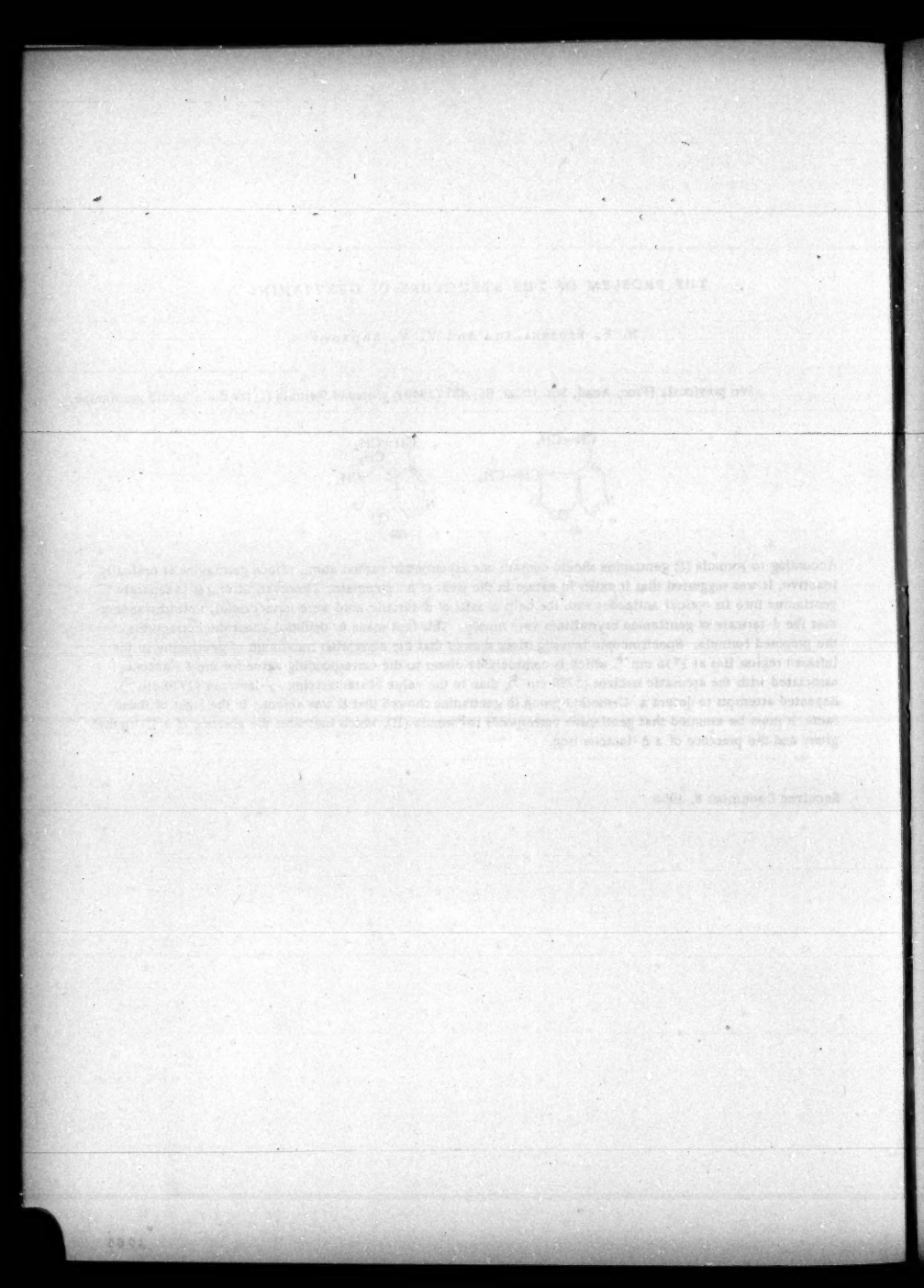
N. F. Proskurnina and V. V. Shpanov

We previously [Proc. Acad. Sci. USSR, 66, 437 (1949)] proposed Formula (I) for the alkaloid gentianine.



According to Formula (I) gentianine should contain one asymmetric carbon atom. Since gentianine is optically inactive, it was suggested that it exists in nature in the form of a racemate. However, attempts to separate gentianine into its optical antipodes with the help of salts of d-tartaric acid were unsuccessful, notwithstanding that the d-tartrate of gentianine crystallizes very nicely. This fact made us doubtful about the correctness of the proposed formula. Spectroscopic investigations showed that the absorption maximum of gentianine in the infrared region lies at 1715 cm^{-1}, which is considerably closer to the corresponding value for the δ-lactone, associated with the aromatic nucleus (1725 cm^{-1}), than to the value characterizing γ-lactones (1770 cm^{-1}). Repeated attempts to detect a C-methyl group in gentianine showed that it was absent. In the light of these facts, it must be assumed that gentianine corresponds to Formula (II), which indicates the absence of a C-methyl group and the presence of a δ-lactone ring.

Received December 8, 1955



RECOLLECTIONS OF N. V. SHISHKIN

December 21, 1954 marked the untimely death of the Director of the Department of Physical Chemistry of the N. G. Chernyshevsky Saratov State University, Nikolai Vasilyevich Shishkin, who was born November 24, 1891.

Nikolai Vasilyevich devoted 36 years of his life to the Saratov University, working there almost from the very start of his careerfirst as an assistant, then as an assistant professor, and finally as a professor.

N. V. devoted many years of his life to the investigation of the nature and genetic interrelationships of unstable complex compounds—iron and aluminum sulfates and iron phosphates. As a result of these investigations, N. V. succeeded in disclosing the nature of a whole group of compositionally complex compounds and establishing a genetic interrelationship between them.

N. V. demonstrated repeatedly that the oxonium ion is a frequently encountered structural element of the lattices of inorganic compounds and suggested a new classification for the water in the empirical formulas for mineral substances, according to which oxonium water is distinguished from other types of water of constitution; he devised a method of detecting oxonium water in the composition of compounds. This method, based on the utilization of the isomorphism of ammonium and oxonium ions, is distinguished by a simplicity and reliability of results that are considerably greater than for other modern scientific methods used for establishing the oxonium structure of substances.

The works of N. V. Shishkin on the investigation of the thermodynamics and formation mechanism of isomorphous mixtures are of great interest. In one section of his doctoral dissertation a theory is developed on the processes of coprecipitation and interaction of isomorphous-salt crystals with their solutions. The views of N. V. introduce much that is new in regard to understanding these processes and clarify a number of problems that are the subjects of discussion of Russian radiologists of Khlopin's school and German radiologists.

Under the direction of N. V. works were also being carried out on the investigation of the surface-adsorption properties of active masses of alkali accumulators. These works are of importance in improving the technology of preparing active masses.

A profound and original scientist, wonderful director and teacher, Nikolai Vasilyevich Shishkin was a man of great character, a very modest, simple and sympathetic person who was loved and respected by all his students and associates.

A. V. Fortunatov, A. S. Kolosov, E. A. Krogius, N. G. Klyukina, A. L. Lvov

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7. Wasserfreie Eisenalaun, Z. anorg. u. allgem. Chem., 245, 226 (1940).

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10. Oxonium Ion in Crystal Lattices of Inorganic Compounds, Sci. Reports, Saratov State University, 24, 21 (1949).

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15. Complex-formation of Ions Fe^{+++} and SO_4^{--} in Solutions, Sci. Reports of Saratov State University, 34, 29 (1954) (jointly with I. G. Shubtsova).

Works Ready for Publication

1. Equilibrium in Quaternary Iron-Sulfate System at 100° (jointly with E. A. Krogius and E. D. Pokhvalensky).

2. Methods of Studying Equilibria in Heterogeneous Salt Systems Containing Isomorphous Mixtures (jointly with B. Sh. Kozel).

3. Determination of the Specific Surface of Nickelous Hydroxide (jointly with N. G. Klyukina).

4. Inorganic Oxonium Compounds (jointly with E. A. Krogius).

5. Nature of Winkler's Salt (jointly with E. A. Krogius and R. S. Videnina).

6. Structure of Basic Nonahydrated Aluminum Sulfate and Alunites (jointly with E. A. Krogius, V. P. Permyakova and G. A. Kudryashova).

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* T. p. = C. B. Translation pagination.

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